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Saturday, August 10, 2013

Welcome and Opening Remarks

Henry Masur, MD, FCCM; Joseph E. Parrillo, MD, MCCM

1. Changes to ABIM's Maintenance of Certification Program

Antoinette Spevetz, MD, FCCM

2. Antibacterial and Antiviral Therapy

Henry Masur, MD, FCCM

3. Principles of Mechanical Ventilation I: Design Features and Mechanics

Neil R. MacIntyre, MD

4. Principles of Mechanical Ventilation II: Clinical Challenges

Neil R. MacIntyre, MD

5. Mechanical Ventilation III: Managing the Ventilator and Weaning

E. Wesley Ely, MD, FCCM

6. Acute Brain Injury and SCCM Guidelines for Pain, Agitation, Delirium

E. Wesley Ely, MD, FCCM

7. Board Review Session I

*E. Wesley Ely, MD, FCCM; Robert Fontana, MD; Neil R. MacIntyre, MD;
Henry Masur, MD, FCCM; Joseph E. Parrillo, MD, MCCM*

8. Difficult Management Problems: ARDS, Mechanical Ventilation, Weaning

E. Wesley Ely, MD, FCCM; Neil R. MacIntyre, MD

9. Life-Threatening Bronchospasm

Neil R. MacIntyre, MD

10. Fulminant Hepatic Failure

Robert Fontana, MD

11. Management of Variceal Bleeding

Robert Fontana, MD

12. Prevention of Nosocomial Infection in the ICU

Daniel J. Morgan, MD, MS

13. Line Sepsis: Prevention and Management

Daniel J. Morgan, MD, MS



**ADULT MULTIPROFESSIONAL CRITICAL
CARE BOARD REVIEW COURSE**

WASHINGTON, DC, USA • AUGUST 10-14, 2013

Society of
Critical Care Medicine
The Intensive Care Professionals



Critical Care Board Review

- **Welcome**
 - 400+ participants from all over US and abroad
- **This is board review**
 - Not an update on new, controversial issues
- **Feel competitive!**
 - Use the audience response system
- **This is a long course**
 - No format makes everyone happy!
 - Take breaks during topics you know
 - Get some exercise

What is the Purpose of the Course

- What is likely to be on the boards
 - We do not know what will be on the boards
 - Many of the faculty have been on the exam committee in the past but they will not reveal anything specific about course content
 - Content emphasis is available to everyone at the ABIM website
<http://www.abim.org/exam/cert/ccm.aspx#content>
 - Dr. Spivetz will present her approach

What Resources Are Provided

- Lectures with embedded questions
- Live Board Review Question Sessions
 - >12 questions per session each day
- Syllabus
- Audioreplay of lectures
 - Available ASAP post course on line
- Website
 - Board type questions with comparison of your answer to your peers

Accuracy of Course Material

- Lectures are by experts
- Questions have been edited and reviewed
- But.....
 - Audience has 400 very smart people
 - If errors appear, let us know
 - Lets not get bogged down on trivia

Critical Care Board Review

- Conflicts of Interest
- Continuing Medical Education
- Pagers and Cell Phones
- ARS System
 - Make sure yours work!
 - Prizes: best daily score, best total score, and the Ironperson Award
- Lets test your ARS system

Appendix

Critical Care Exam Pass Rate for Initial Certification, First Time Takers

Year	#	% Pass
2005	423	90%
2006	471	92%
2007	488	91%
2008	549	88%
2009	443	92%
2010	531	94%

Critical Care Exam Pass Rate for Recertifiers

Year	#	% Pass
2006	250	94%
2007	528	95%
2008	295	88%
2009	469	93%
2010	406	94%

Critical Care Exam Blueprint

Subject Area	%	#
Pulmonary Disease	22.5%	46-51
Cardiovascular Disorders	17.5%	26-35
Renal/Endocrine/Metabolism	15%	30-34
Infectious Disease	12.5%	23-25
Neurologic Disorders	7.5%	12-16
Surgical/Trauma/Transplantation	7.5%	11-15
Gastrointestinal Disorders	5%	8-11
Hematologic/Oncologic Disorders	5%	10-11
Pharmacology/Toxicology	5%	9-10
Research/Administration/Ethics	2.5%	5-10
Total	100%	200



American Board
of Internal Medicine

Changes to ABIM's Maintenance of Certification Program

Antoinette Spevetz, MD, FCCM, FACP

Associate Professor of Medicine

Designated Institution Official

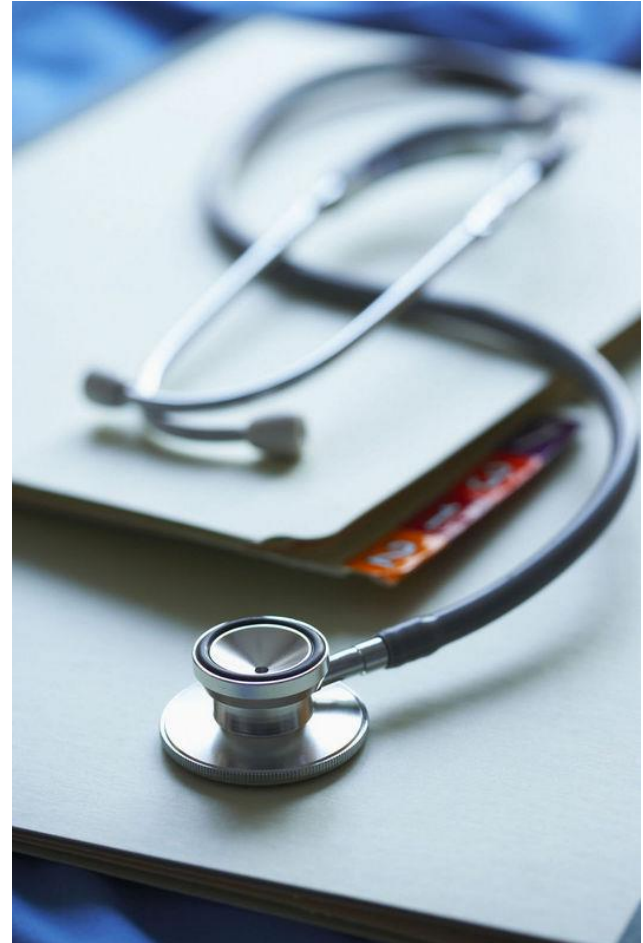
Cooper University Hospital

Cooper Medical School of Rowan University

Specialty certification:

A unique strength of US medical professionalism

- Independent of membership societies
- Voluntary, independent, non-governmental
- American Board of Medical Specialties: 24 approved medical specialty boards



Reducing redundancy

- ABIM is committed to continuously evaluating the program and ensuring that our assessments are:
 - as unburdensome as possible;
 - as authentic as can be; and
 - as harmonized with other requirements as possible.
- ABIM knows most physicians are already engaged in professional self-assessment and improvement.



Why is ABIM changing MOC?

- The American Board of Medical Specialties (of which ABIM is a member) is requiring more frequent engagement of diplomates in MOC activities: all Boards are required to develop a **continuous MOC program**.



Why is ABIM changing MOC?

Every 10 Years is not enough

“The growing knowledge base requires that training and ongoing licensure and certification reflect the need for lifelong learning and evaluation of competencies.”

National Research Council. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, DC: The National Academies Press, 2001.

What is “Meeting MOC Requirements”?

- In January 2014 – ABIM will begin reporting whether or not physicians are “Meeting MOC Requirements.”
 - Everyone holding a current certificate and valid license will be meeting requirements at the program launch.
- You will remain board certified regardless of your participation in MOC – until your current certification expires.

What are the new requirements?

- If you aren't already enrolled in MOC, do so by March 31, 2014 to remain "Meeting MOC Requirements."
- By December 31, 2015, complete an MOC activity, either offered by ABIM or another organization, to earn ABIM MOC points to be reported as "Meeting MOC Requirements."
- By December 31, 2018, earn a total of 100 MOC points in a mix of Self-Evaluation of Medical Knowledge and Self-Evaluation of Practice Assessment modules (as well as complete the new patient safety and patient survey requirements).

Patient Safety & Patient Survey Requirements

- Currently one option to meet patient safety requirement: the ABP-lead Joint Primary Care Board product.
- Developing process to meet requirement with patient safety related activities at institutions.
- Will be adding many more patient safety options.
- PIMs with a patient survey will count toward patient survey requirement.
- Will offer options to meet requirement without doing a full PIM.
- Developing process to approve surveys already in use.

• **Diplomates have until December 31, 2018 to meet the Patient Survey and Patient Safety requirements**

What else will be different about MOC?

- Redesign of infrastructure/IT platform to be more user friendly (and allow for easier voluntary data exchange)
- Earn MOC points for taking an exam
- Flexible fee structure – annual payment option
- Grace periods for newly certified and physicians in fellowship

How much will it cost after the program launches?

MOC in Internal Medicine

around \$200 per year

Subspecialty MOC

around \$250 per year

- If you are enrolled in MOC most diplomates will not owe anything until their current enrollment expires.
- Cost to maintain more than one certification will be the fee of the most expensive certification plus half for each of the others.
- Options to pay annually or pre-pay 10 years.
- Newly certified diplomates in internal medicine will receive a 1-year fee waiver.
- Diplomates in fellowship will receive an MOC program fee credit after every successful fellowship year completed.
- Fee includes one MOC exam for each certification you are maintaining. (Exam re-takes are \$775.)
- **All ABIM modules are included in the fees. Diplomates can complete as many as they would like and earn CME without additional costs.**

Listening to diplomates

What we learned from focus groups conducted with diplomates:

- ✓ Diplomates would like a great deal of personalized guidance and reminders to stay on track.
- ✓ Diplomates want to succeed in MOC, whatever the requirements.

Changes to MOC:

- ✓ ABIM will develop messages that strongly encourage physicians to visit the ABIM Physician Portal, early and often.
- ✓ Clear communication to everyone who helps physicians manage their MOC requirements.

The message from diplomates is loud and clear:

“Just tell me what to do!”



MOC Program Status

Point Requirements

Requirements

Points Earned

100

20 pts. in Practice Assessment ⓘ by 12/31/2017

Plan Ahead! This can take up to 6 months!! ⓘ

0 of 20

20 pts. in Medical Knowledge ✓ **DONE**

20 of 20

60 Elective ⓘ **pts. (any category) by 12/31/2017**

Earn 30 of these by 12/31/2017

Points that will be earned by taking exams: **40**

10 of 60

0

Exams and Other Requirements

Patient Survey ✓ **DONE**

Patient Safety Module ⓘ

Due by 12/31/2017

Internal Medicine EXAM ⓘ

Pass by 12/31/2017

Plan Ahead! Registration closes 3 months
before exam date! ⓘ

Cardiology EXAM ⓘ

Pass by 12/31/2017

Plan Ahead! Registration closes 3 months
before exam date!

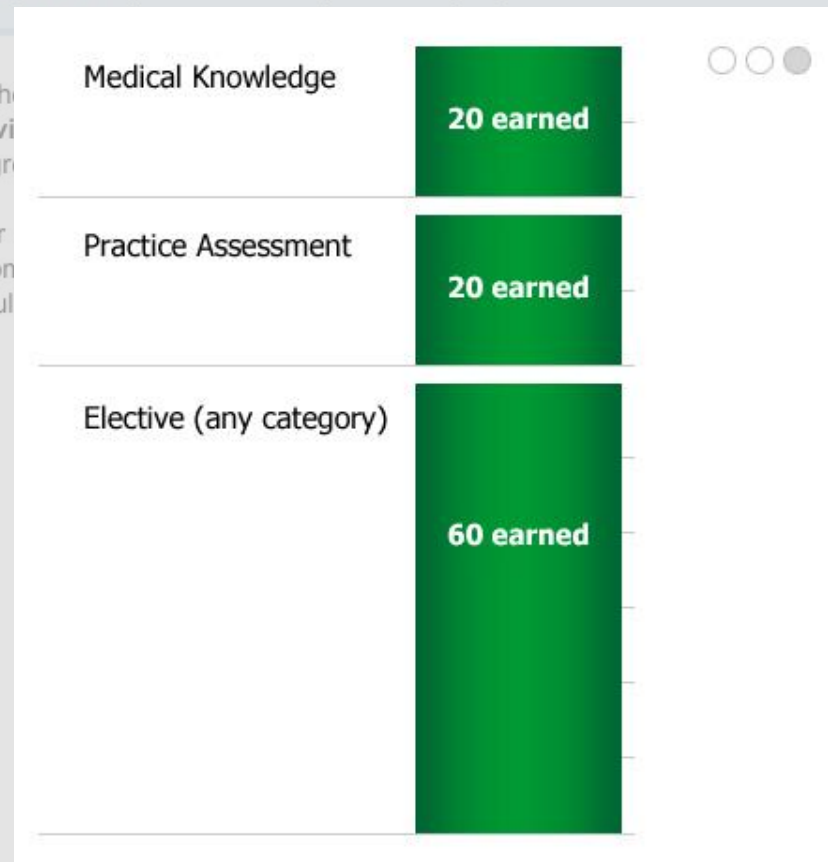
Your personal guide to your MOC program:

ABIM plans to send all diplomates an e-mail upon launch with details on how to activate your program. [Make sure your e-mail is up-to-date in our system](#) so you are sure to get this very important communication.

As the
provi
progr

Your
recon
shoul

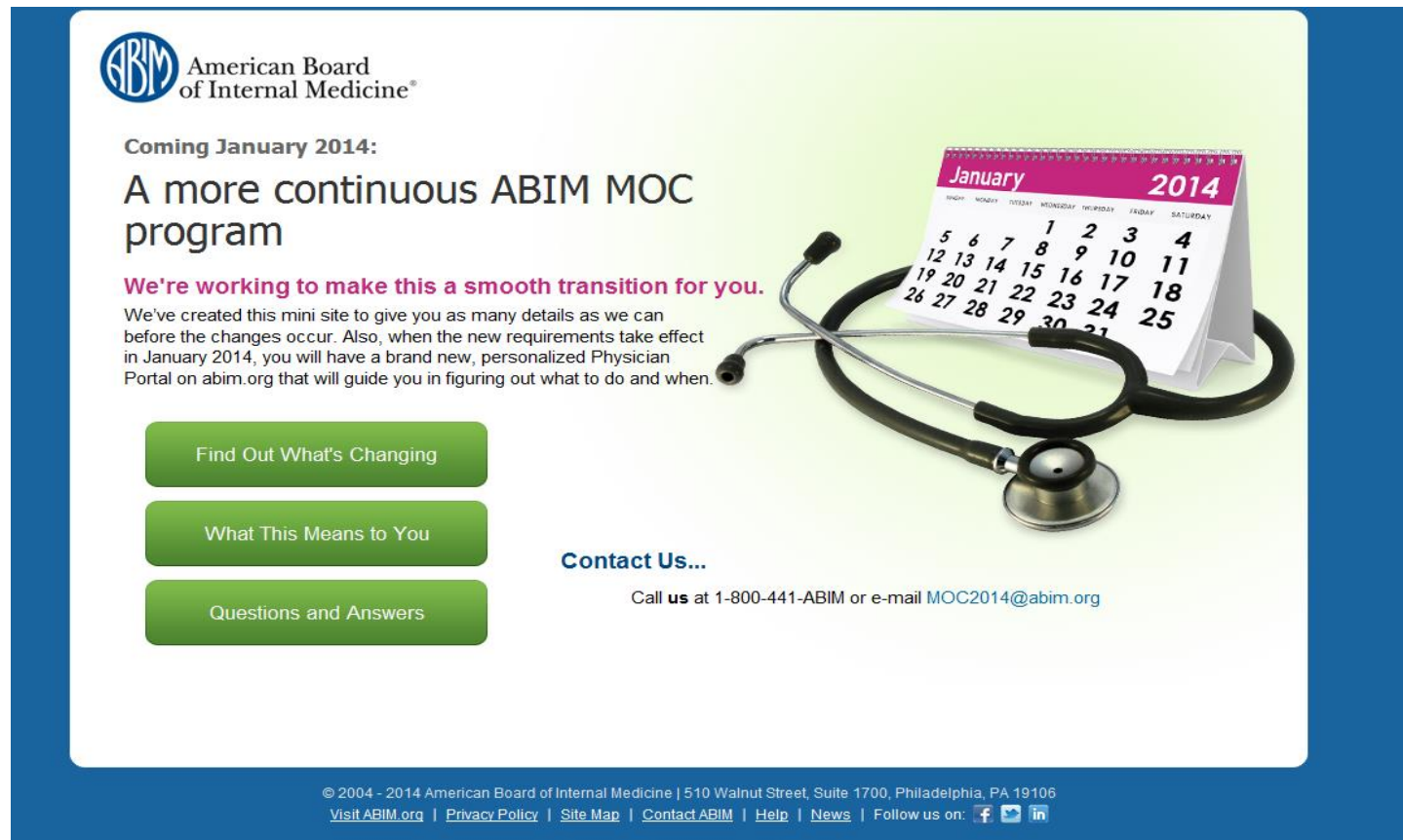
t you



This is a preview of the new MOC Program status overview that we will be implementing.

I want to know about my particular situation:

- Visit moc2014.abim.org to help answer any questions about the new MOC requirements.

A screenshot of the American Board of Internal Medicine (ABIM) website for the MOC 2014 program. The page has a light green background with a blue border. At the top left is the ABIM logo and the text "American Board of Internal Medicine®". Below this, it says "Coming January 2014:" followed by the heading "A more continuous ABIM MOC program". A paragraph of text explains the transition to a new Physician Portal in January 2014. To the right of the text is a graphic of a stethoscope and a calendar for January 2014. Below the text are three green buttons: "Find Out What's Changing", "What This Means to You", and "Questions and Answers". To the right of these buttons is a "Contact Us..." section with the phone number 1-800-441-ABIM and the email address MOC2014@abim.org. At the bottom of the page is a footer with copyright information and links to various resources.

ABIM American Board of Internal Medicine®

Coming January 2014:

A more continuous ABIM MOC program

We're working to make this a smooth transition for you.

We've created this mini site to give you as many details as we can before the changes occur. Also, when the new requirements take effect in January 2014, you will have a brand new, personalized Physician Portal on abim.org that will guide you in figuring out what to do and when.

[Find Out What's Changing](#)

[What This Means to You](#)

[Questions and Answers](#)

Contact Us...

Call us at 1-800-441-ABIM or e-mail MOC2014@abim.org

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Rollout of the new requirements

- Spring 2013 – Diplomates notified about changes.
- Summer 2013 – Diplomates receive reminders about changes.
- January 2014 – Access to new ABIM Physician Portal.
 - All diplomates who are in good standing will be “Meeting MOC Requirements” at launch.
- March 31, 2014 – Diplomates need to activate their MOC program and pay any outstanding MOC fees.
- December 31, 2015 – Complete an MOC activity to continue to be “Meeting MOC Requirements.”



What's not changing?

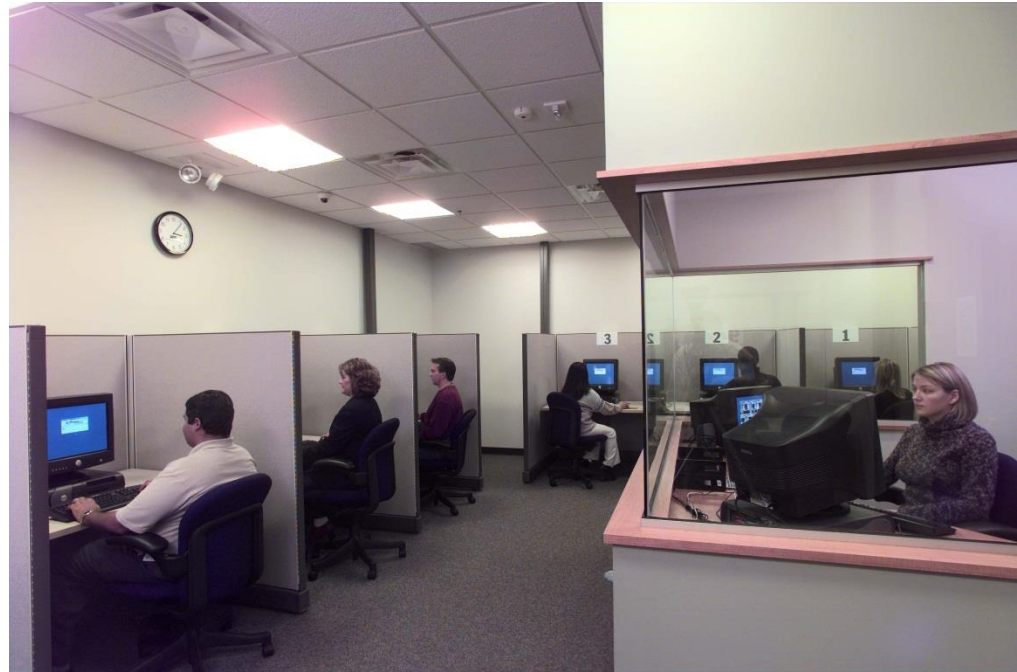
- You will still have the ability to earn points by working in groups, participating in Learning Sessions and receiving credit for approved society products; however, the patient safety and patient survey requirements are new.
- How you meet the Self-Evaluation of Medical Knowledge and Self-Evaluation of Practice Assessment requirements isn't changing.
- You must still take an MOC exam every 10 years.

Components of MOC

- Secure Exam
- Self-Evaluation of Medical Knowledge
- Self-Evaluation of Practice Assessment
- Patient Survey Module
- Patient Safety Module

The Secure Exam

- Constructed and developed with similar approach as initial certification exams.
- Focus is on diagnosis, prognosis, therapeutic goals and not so much on basic science and emerging therapies.
 - Eventual pass rate 96%¹



¹ABIM MOC exam pass rates 1996-2010

Self-Evaluation of Medical Knowledge

- ABIM Self-Evaluation products
 - Annual Updates Critical Care Medicine, Pulmonary Disease, Internal Medicine [3 available in each area every year]
 - Clinical Skills
 - Care for the Underserved
 - Point of Care
 - Patient Safety Modules
 - Other approved products offered by medical societies and other organizations
 - **SCCM's Adult Multiprofessional Critical Care Review Course**
 - Visit www.abim.org for a complete list.

Self-Evaluation of Practice Assessment

I know I have to do this, but I do not have data that I trust that tells me anything useful about my practice performance.



**“Classic” PIMs
(Practice Improvement
Modules)**

I have valid performance data using evidence-based measures, but I need a tool to support my QI project (or would like to report a project that is already completed).



**Self-Directed PIM
or
Completed Project
PIM**

I’m involved in a quality improvement project that has been pre-approved by ABIM for practice performance credit.



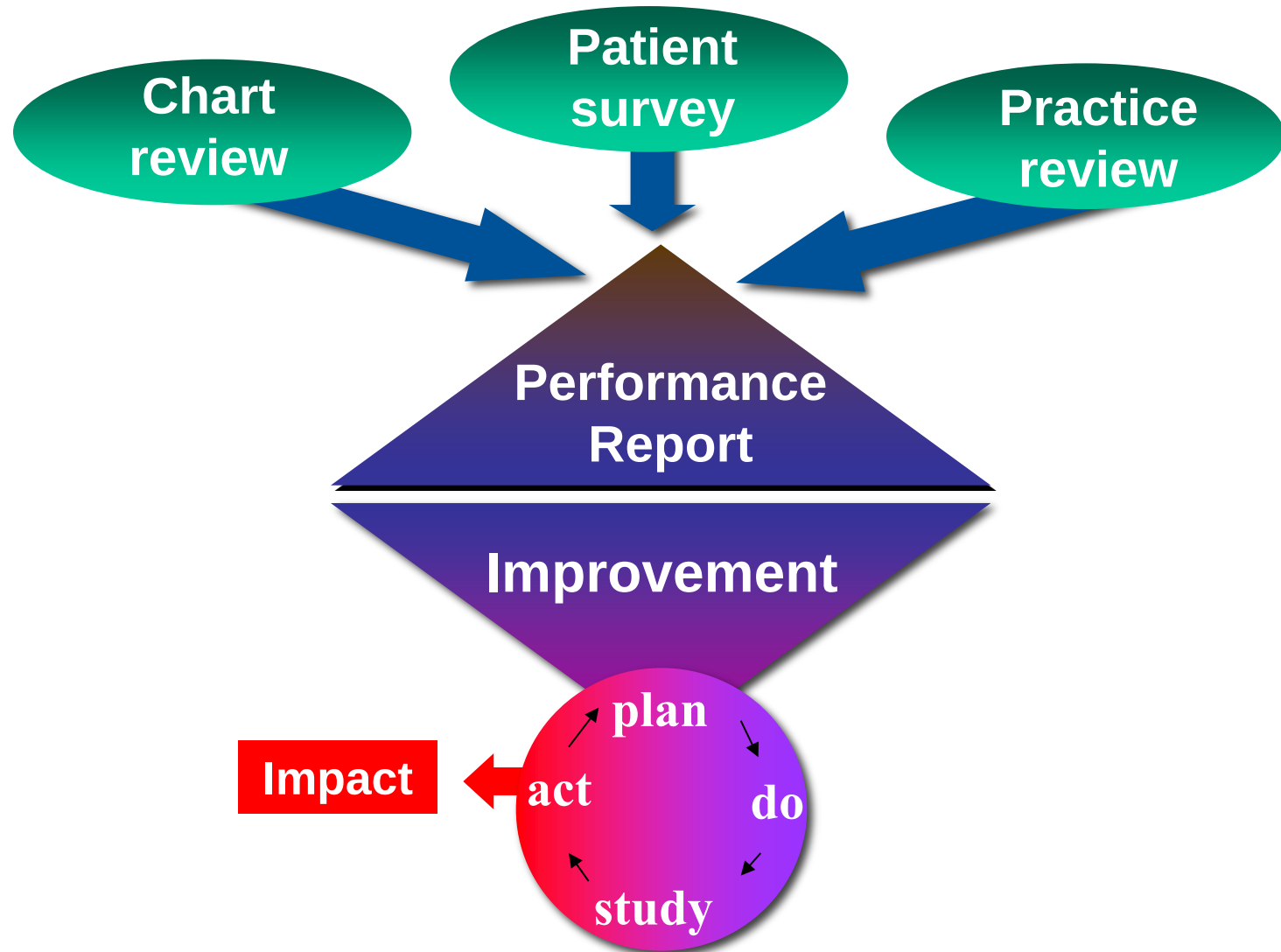
AQI Program

I don’t practice clinical medicine.



**Essentials of QI Module
(for clinically inactive
physicians)**

Practice Improvement Module



Growing number of PIMs

PIMs for Critical Care Subspecialists

- Asthma*
- Chronic Obstructive Pulmonary Disease PIM
- Clinical Supervision
- Communication
 - Primary Care*
 - Subspecialists*
 - Recent Visit*
 - Referring Physicians
- Completed Project (using approved quality measures)
- Self-Directed (using approved quality measures)
- Approved Quality Improvement (AQI) Modules
- Essentials in Quality Improvement (EQI) for the clinically inactive
- Visit www.abim.org for a complete list.

***Includes patient survey**

Ways to complete PIMs

- By yourself or in a group. Your entire practice can complete as a team.
 - Full point credit for the module for each diplomate participating in MOC.
- With residents or fellows as a PIM in Residency.
- By using data/measurements from medical societies/other sources.
- By using data from your own practice.



Self-Directed and Completed Projects PIMs

- The SD & CP PIMs allow physicians or groups of physicians to use validated performance data to report on or begin a quality improvement activity.
- Process:
 1. Collect data.
 2. Make a plan for improvement.
 3. Test the impact of your plan.

Using measures in the Self-Directed PIM

 PRACTICE IMPROVEMENT MODULE® *ABIM MEASURES LIBRARY*

HelpSave & Quit

✓ PART A
Orientation

✓ PART B
Measures & Data

✓ Search the Measures Library

Exit or Search Again

Search the Measures Library

CHOOSE A MEASURE SET FROM THE LIBRARY
Measures are organized into sets that often appear together on a quality report. Search the library to find a set that includes the same measures as those on your report. A measure set may be selected already. To search for a different measure set, select *Search a condition* or use the *Search by keyword* option.

Critical Care Medicine

No sub-topics are available

or

Search by keyword

SEARCH

+ Central Line-Associated Bloodstream Infections

+ Inpatient CAP: Community-Acquired Pneumonia 

+ Intensive Care

+ Sepsis

+ VTE: Venous Thromboembolism

Approved Quality Improvement Pathway

- **AQI Options for Pulmonology, Critical Care, and Sleep Medicine**
 - ATS: PFT Improvement Series: Collaborating for Accelerated Change
 - ACCP: Performing EBUS-TBNA to Diagnose NSCLC
 - ACCP: Venous Thromboembolism (VTE) Prophylaxis Performance Improvement Project
- Visit www.abim.org/tool for a complete list.

ABIM's aim: To harmonize MOC with real-life practice and other imperatives

- Today
 - Help in staying current.
 - Opportunity to earn CME credit.
 - An aid in meeting some hospitals' and medical groups' privileging requirements.
 - Recognition in certain health plan physician directories and inclusion in quality-tiered networks.
 - A marker of professionalism.

- A likely future
 - Counts for Maintenance of Licensure (MOL).
 - Included in increasingly robust public and private physician ranking/assessment systems.



Need help?

- Looking for more information about the new MOC program requirements? Access the official site at moc2014.abim.org
- Not enrolled in MOC? Log in to www.abim.org and complete the online enrollment.
- Checking your MOC status? Log in to www.abim.org to view your MOC Status Report.
- Have questions?
 - Call ABIM's Diplomate Services Department, 800-441-ABIM (2246).
 - E-mail us at: request@abim.org
 - Go online to: <http://www.abim.org/moc/>

Antibacterial and Antiviral Therapy 2013

Henry Masur, MD, MACP, FCCM
Bethesda, Maryland

Conflicts of Interest

- No conflicts of interest
- Much of the discussion will involve off-label use of antibiotics

Update on Antibacterial and Antiviral Therapy

- Antibacterial
 - Gram Positive Cocci
 - Gram Negative Bacilli
 - Anaerobes
- Antiviral
 - Herpes viruses
 - Respiratory viruses

Gram Positive Cocci

Case 1

- 42 year old lawyer developed two furuncles on his arm which became progressively red and tender over the past 48 hours.
- He presents to the ER after a syncopal episode: he is febrile and hypotensive. He is transferred to the ICU from the ER with septic shock
- After obtaining appropriate cultures, you would initiate meropenem plus:
 - a) Vancomycin
 - b) Linezolid
 - c) Tigecycline
 - d) Daptomycin
 - e) All of the above would be adequate

Gram Positive Cocci

- Staphylococcus aureus
- Streptococcus pneumoniae

MRSA Strains in U.S. Were Distinct but Are Now Merging

	Healthcare	Community
Prevalent genotypes	USA100 USA200	USA300* USA400
Antimicrobial resistance	Multiple	Few
SCC<i>mec</i>	Types I-III	Types IV, V
PVL toxin gene	Rare	Common

What Drugs Are Active Against MRSA?

- Vancomycin
- Linezolid
- Daptomycin
- Tigecycline
- Clindamycin
- Doxycycline
- Trimethoprim-Sulfamethoxazole

Antistaphylococcal Penicillins

Drug

Methicillin

Nafcillin

Oxacillin

Toxicity

(No longer marketed)

Leucopenia (> 2 weeks)

Hepatitis

How Should You Treat Serious Oxacillin Sensitive *Staphylococcus aureus* Infections?

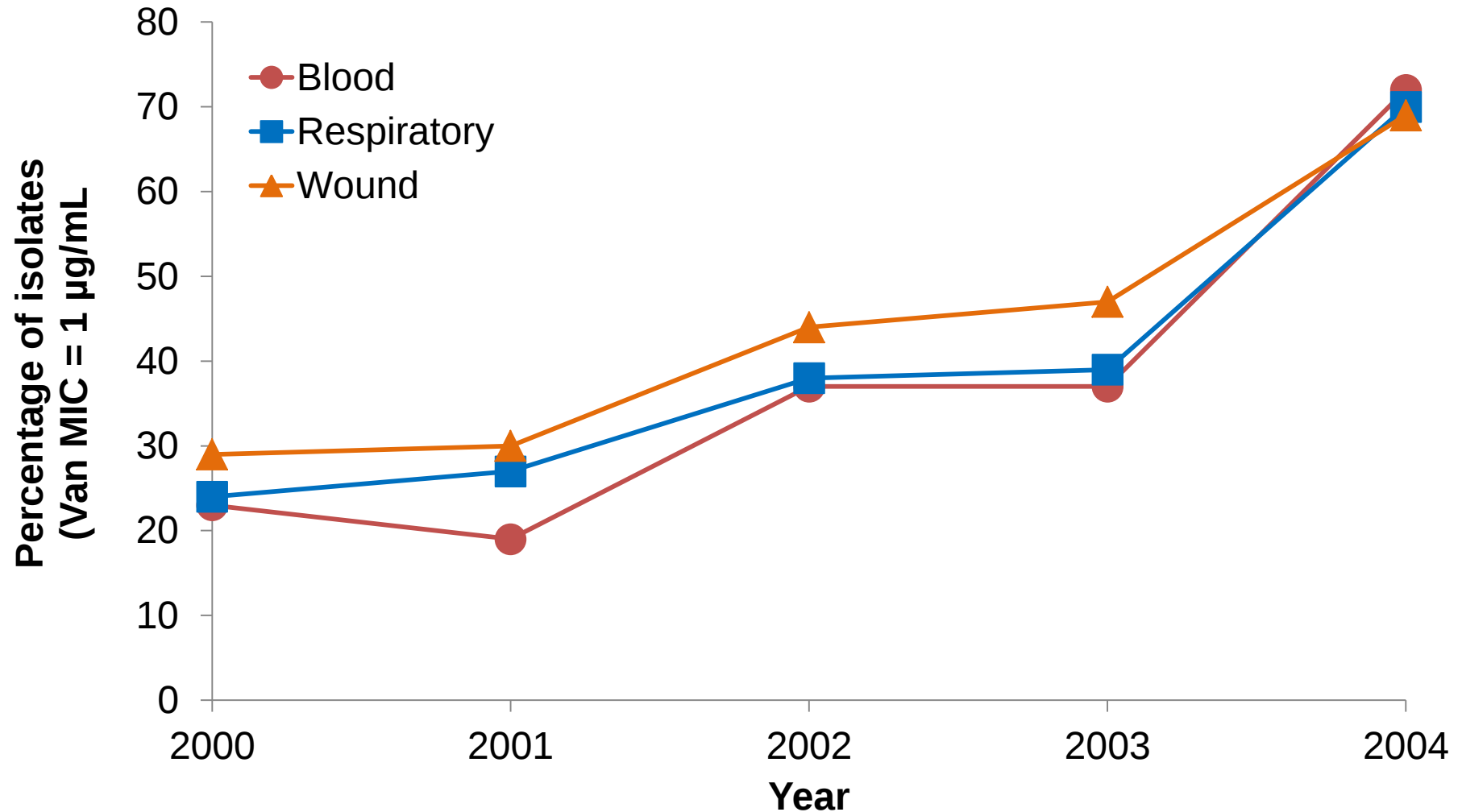
- Oxacillin is preferable to Vancomycin
- Penicillin allergic:
 - Desensitize if possible
 - Vanco is conventional
 - Linezolid (but probably NOT tigecycline) can be used)(static)
 - Daptomycin is cidal and MIGHT be preferable
- Combination therapy for MSSA may be useful
 - Gentamicin
 - Reduces bacteremia by 1 day
 - No difference in outcome
 - Do not use > 3-5 days
 - Rifampin
 - No ↑ cidal activity
 - May be useful with foreign bodies
 - *Emerging controversies about outcome*

Vancomycin

- Broad activity vs aerobic gram pos cocci
 - Inactive against anaerobes, gram negatives
 - Resistance: VRE (common), VRSA (very rare)
- Dosing
 - Load with 25-30mg/kg (2g for 70kg), then 15-20mg/kg q 8-12h
- Poor penetration
 - Lungs
 - CNS after steroids (pearl: use 2g q12h!!-push levels)
- Resistance: Amazing!
 - 3 cases in 30+ years
 - No drug is proven superior for MRSA!
- Renal elimination
- Toxicities: Renal, Otic, occasional leukopenia, ITP
- Avoid empiric use esp > 3 days

Percent of Staph aureus with Vancomycin MIC >1

VISA, VRSA Are Not Easily Testable for CCM



Is Vancomycin Resistant MRSA on the Horizon?

- Vancomycin resistance
 - 8 Unrelated isolates
 - 2 had Van A (probably from *E. fecium*)
- Vancomycin clinical failure
 - Correlates with higher MIC
- Vancomycin Intermediate (VISA)
 - Vanco MIC 4-8ug/ml
 - All MRSA
 - Accessory Gene Regulator (agr) II, not Van A

Do You Need to Draw Vanco Levels?

- Reasons
 - Unpredictability in ICU re renal function
 - Assure efficacy
 - Reduce toxicity (renal, otic)
- Goals
 - Trough 15-20 ug/ml measured after 4th dose
 - (Higher troughs correlate with more nephrotoxicity)

Linezolid

- Dose: 600mg IV / PO BID
- No adjustments for liver or renal disease
- Adverse effects
 - *Bone marrow suppression
 - (leukopenia and thrombocytopenia after >12 days)
 - Long term use: peripheral neuropathy and optic neuritis
 - (e.g. for mycobacterial disease)
 - Serotonin syndrome, lactic acidosis
- Penetration into lungs, CNS
 - High ratio CSF or BAL: serum
- Concerns about use
 - Bacteremia
- Possibly preferable to Vanco
 - ORSA Pneumonia
 - Skin and soft tissue
 - Inhibits toxin release (as does clinda)

Question

To treat life threatening Staphylococcal pneumonia, which of the following would be expected to be INACTIVE?

- a) Vancomycin
- b) Linezolid
- c) Daptomycin
- d) Tigecycline

Daptomycin

- Bactericidal
- Active against almost all Gram Pos Cocci
- Well tolerated
- Dose adjust: Cr Cl < 30
- Available only IV
- Few drug interactions
- Indicated: skin/soft tissue and bacteremia
- Problem
 - Poor penetration into lung/surfactant binding
- Limited data on CNS penetration or efficacy for meningitis
- 2013: MIC Creep

Eosinophilic Pneumonia & Daptomycin



U.S. Department of Health & Human Services



U.S. Food and Drug Administration

[Home](#) > [Drugs](#) > [Drug Safety and Availability](#) > [Postmarket Drug Safety Information for Patients and Providers](#)

Drugs

FDA Drug Safety Communication: Eosinophilic pneumonia associated with the use of Cubicin (daptomycin)

[Safety Announcement](#)

[Additional Information for Patients](#)

[Additional Information for Healthcare Professionals](#)

[Data Summary](#)

Safety Announcement

[07-29-2010] The U.S. Food and Drug Administration (FDA) is informing patients and healthcare professionals about the potential for developing eosinophilic pneumonia during treatment with Cubicin (daptomycin), an intravenous antibacterial drug.

Empiric Therapy of Choice for Staphylococcus aureus Bacteremia

- Vanco
- Vanco Plus Oxacillin
- Daptomycin
- NOT LINEZOLID

Staph aureus Bacteremia

- Key Issue: Complicated or Uncomplicated?
- For the boards
 - Longer duration of therapy is always better
- For clinical practice
 - Always remove catheter asap
 - What are the criteria that justify only 14 days rx

Uncomplicated Catheter-Associated Staph aureus Bacteremia that Can Be Treated for Only 14 Days

- All Catheters removed/replaced
- Defervesce in 72h
- Not Immunosuppressed
(not neutropenic or diabetic)
- Blood cultures negative by 72 hrs
- No intravascular prosthetic material (pacer, valve)
- TEE negative for vegetations (day 5-7)
- Ultrasound negative for thrombophlebitis
- Phys Ex neg for metastatic infection

Treatment of Bacteremic Staph Aureus Disease

- Choice of Drug
 - MSSA: Beta – lactams >> Vancomycin
 - MRSA:
 - Bacteremia: Vancomycin, Daptomycin
 - Pneumonia: Vancomycin, Linezolid
- Combination Therapy with Rifampin
 - Only if prosthetic device is present (retained or replaced)
- Combination with gentamicin
 - Optional for 3-5 days to reduce duration bacteremia
- Duration
 - Uncomplicated: 2 weeks
 - Complicated: 4-6 weeks

Look for Complications of Staph aureus Bacteremia

- Endocarditis
 - TEE, not TTE, is gold standard
- Back pain
 - Look for vertebral osteomyelitis or epidural abscess
- Joint pain
 - Look for septic arthritis
- Leg weakness/incontinence
 - Look for epidural abscess
- Cardiac device or any prosthesis
 - Removal is always preferred

How Worried Should You Be About Penicillin Resistant Pneumococci?

- PCN Resistant: MIC > 2.0
- Clinical Failures
 - Pneumonia
 - Rare if PCN or ceftriaxone used
 - Cefuroxime failures more common
 - Meningitis
 - Quinolone failures have been reported
 - Penicillin failures also reported
- When in Doubt
 - Use Vancomycin or Linezolid

Should Cefepime Be Used?

Cefepime

- Indications
 - Bacteremia, Pneumonia, Skin/Soft Tissue
 - Febrile neutropenia, UTI, Gyn, Abdominal
- Gram Positive Cocci
 - Enhanced activity including MRSA and Pneumococcus compared to ceftazidime
- Gram Negative Rods
 - Enhanced activity against Extended spectrum beta lactamase producing rods
 - Better cell wall penetration
 - Less affinity for some beta lactamases
 - Binds to multiple penicillin binding proteins

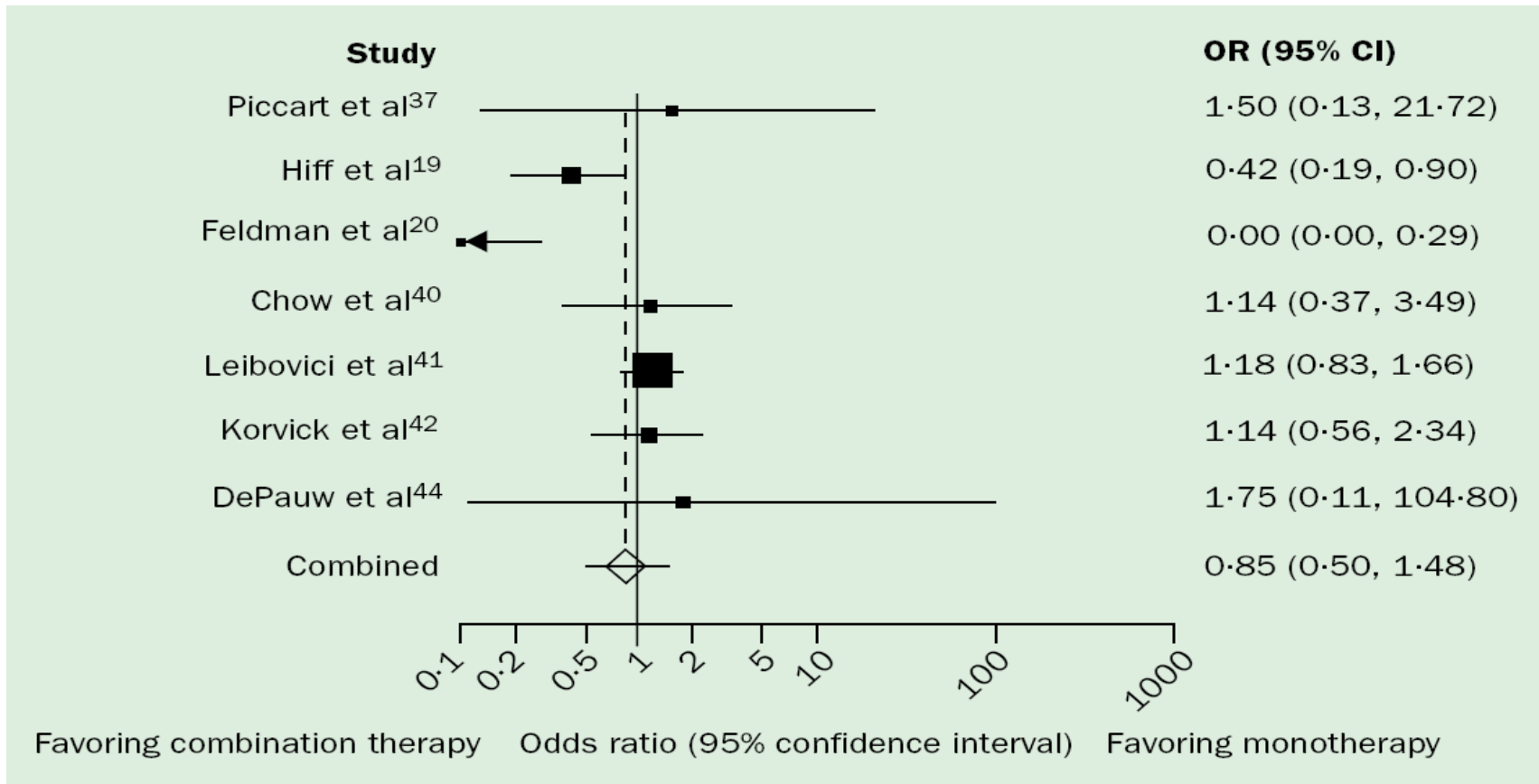
 Efficacy and safety of cefepime: a systematic review and meta-analysis

Dafna Yahav, Mical Paul, Abigail Fraser, Nadav Sarid, Leonard Leibovici

Difficult Gram Negative Infections

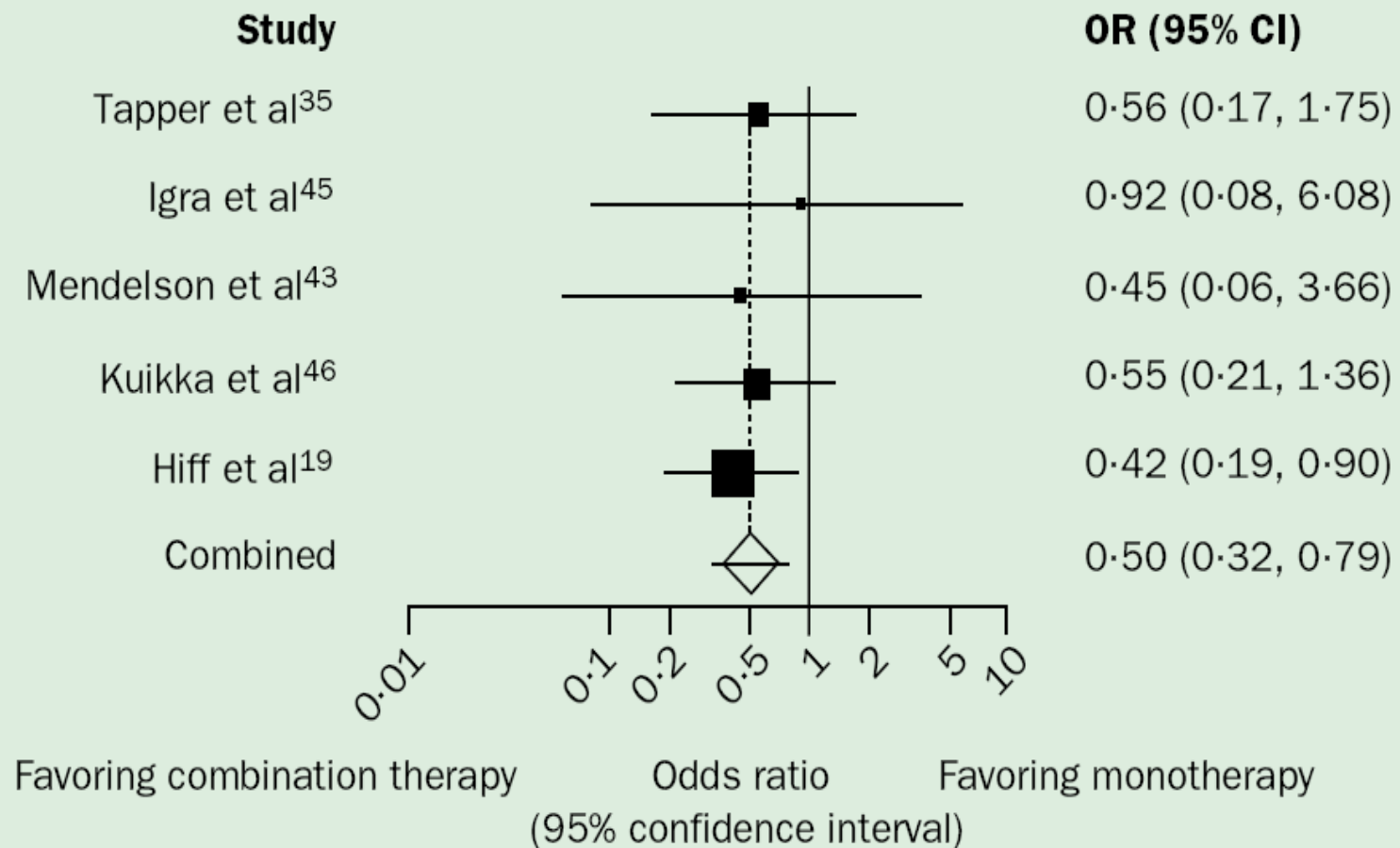
Monotherapy vs Combination Therapy for Gram Negative Bacteremia: Prospective Studies

No Reason to Use Combination Therapy Once Susceptibility Known



Monotherapy vs Combination Therapy for Gram Negative Bacteremia: Pseudomonas

Maybe Combination Therapy Justified



Issues in 2013 for Gram Negative Rods

- Extended spectrum beta lactamases
- Multiply resistant ESBL producers
 - Concurrent resistance to Aminoglycosides, Fluoroquinolones
- Carbapenemases

Question

Which of the following organisms is least likely to be susceptible to Imipenem?

- a) Staph aureus
- b) Strep pneumoniae
- c) Enterococcus fecium
- d) Bacteroidis fragilis
- e) Pseudomonas aeruginosa

Carbapenems

Drug	S. Aureus	MRSA	Strep	Enterococ	GNR	Anaerobe	Pseudo
Imipenem	4+	0	4+	Fecalis (Not Fecium)	3+	4+	3+
Meropenem	4+	0	3+	Fecalis (Not Fecium)	4+	4+	3+
Ertapenem	3+	0	4+	Fecalis (Not Fecium)	4+	4+	0
Doripenem	3+	0	4+	Fecalis	3+	4+	4+

Which Carbapenem Should You Use?

- | | |
|-------------|---|
| • Imipenem | The Standard |
| • Meropenem | Fewer seizures (probably) |
| • Doripenem | Best Pseudomonas coverage |
| • Ertapenem | No Pseudomonas coverage
Fewer seizures
QD, IV, IM |

Fluoroquinolones

Urinary, GI

GPC Activity

Enterococci

Anaerobes

GNR

Pseud

Norfloxacin

+

-

-

+/-

-

Ciprofloxacin

+/-

-

-

++

+

Respiratory

GPC Activity

Enterococci

Anaerobes

GNR

Pseud

Levofloxacin

+

-

-

+

+

Moxifloxacin

+

-

-

+

-

Quinolones

- Remember
 - No activity against MRSA, Enterococcus
 - Only Moxi has activity (some) against anaerobes
 - Flagging activity against Gram negative rods
- Pneumonia
 - Active
 - Pneumococcus, Legionella, Chlamydia, Mycoplasma
 - Moxifloxacin or Levofloxacin (750 mg in ICU)
- Gram Negative Infections
 - Active but resistance is increasing
 - Pseudomonas, E. Coli, Klebsiella, etc
 - Cipro or Levofloxacin (750mg in ICU)
- Meningitis
 - Do not use quinolones

Class Toxicities of Quinolones

- Lower seizure threshold
- Altered mental status
- Achilles rupture
- Rash
- Prolonged QT
- Hypoglycemia (Gatifloxacin)

Aminoglycosides

- Concentration dependent killing
- Renal and ototoxic
- Dosing: Gentamicin 5-8 mg/kg q24h
Amikacin 15 mg/kg q24h
- OD Dosing:
 - Less nephrotoxic
 - May be more effective
- Legal Issues
 - Some experts refuse to use them
 - Use for short courses

Polymyxins

- Developed 1950-1960
- Active
 - Pseudomonas/Acinetobacter
 - Other gram negative rods
- Nephrotoxic/ototoxic/neurotoxic
 - Use curtailed in 1970's
- Polymyxin-B
 - Mainly topical
- Polymixin-E (Colistin)
 - Used parenterally as colistimethate

Polymyxin E (Colistin): Dosage

- No large studies on efficacy or toxicity
- Current use:
 - 2.5 – 5.0 mg/kg/day in 2-4 divided doses
 - not to exceed 300 mg/d
- Safety, efficacy, optimal dose uncertain

Polymyxin Toxicity

- Nephrotoxicity
 - Incidence 5%
- Neurotoxicity
 - Incidence 30%
 - Perioral paresthesia
 - Ataxia
 - Reversible

Tetracyclines and Glycylcyclines

- Doxycycline
- Minocycline
- Tetracycline
- Tigecycline

Tigecycline: Microbiologic Activity

- Gram Positive Cocci
 - Staph aureus (MSSA and MRSA)
 - Streptococci
 - Penicillin resistant Pneumococci
 - Enterococci
 - VRE
- Gram Negative Bacilli
 - E. Coli
 - Klebsiella
 - Stenotrophomonas
- Anaerobes
 - Bacteroides
- **NOTE: Not active against 3 Ps!!**
 - Proteus
 - Providencia
 - Pseudomonas

Tigecycline Toxicities

- Nausea, Vomitting
- Hepatitis
- Pancreatitis
- Catabolic state (BUN rise)
- Pseudotumor cerebri

Antimicrobial Agents with Activity Against Anaerobes

Drug	Respiratory	Abdominal
Penicillin	+	-
Clindamycin	+	-
Metronidazole	+	+
Cefoxitin/Cefotetan	+	+/-
Ampicillin -Sulbactam	+	+
Ticarcillin - Clavulanate	+	+
Piperacillin - Tazobactam	+	+
Imipenem or Meropenem	+	+

Which Antibacterials Can Be Given By Rapid Infusion

<u>Drug</u>	<u>Minimum Infusion</u>
Pen G	60-120 min
Pip-tazo	20-30 min
Ticar-clav	30 min
Cefepime	30 min
Daptomycin	10 min
Meropenem	3-5 min
Imipenem	20-30 min
Ertapenem	30 min
Doripenem	60 min

Antiviral Therapy for Intensivists

- Herpes viruses
 - HSV
 - CMV
- Respiratory viruses
 - Influenza
 - Respiratory syncytial virus

Herpes Viruses

- Herpes simplex virus, type 1 (HSV-1)
- Herpes simplex virus, type 2 (HSV-2)
- Varicella-zoster virus (VZV)

- Cytomegalovirus (CMV)
- Human herpes virus 6 (HHV 6)
- Human herpes virus 7 (HHV 7)

- Epstein-Barr virus (EBV)
- Human herpes virus 8 (HHV 8)

Question

What is the drug of choice for Herpes simplex encephalitis in an immunologically normal 20 year old previously in good health?

- a) Acyclovir alone
- b) Acyclovir plus corticosteroids
- c) Ganciclovir
- d) Foscarnet
- e) Cidofovir

Antiviral Drugs for HSV,VZV

- Acyclovir
 - Dose for dissemination, encephalitis is 10/mg/kg q8h instead of 5mg/kg tid
 - Toxicity
 - Renal crystals/stones
 - Resistance rare except in transplants, HIV who are on chronic suppression
 - Ganciclovir, Foscarnet if resistant

Parenteral Drugs for CMV

- Ganciclovir
 - Drug of choice
 - Toxicities: marrow suppression
 - Resistance occurs
- Foscarnet
 - Alternative choice
 - Toxicities: nephrotoxic, seizures, chelation of cations (Mg, Ca)
 - Resistance occurs but is rare

Question

A 35 year old male is 6 weeks post human stem cell transplant for AML. He is admitted to the ICU with respiratory failure after 2 days of fever and cough.

Rapid RSV test on nasopharyngeal wash is positive

Which of the following has been shown to be effective for this patient's RSV pneumonia?

- a) Aerosol Ribavirin
- b) IV Ribavirin
- c) Palivizumab
- d) Aerosol ribavirin plus palivizumab
- e) None of the above

Drugs of Choice for Respiratory Viruses

- RSV
 - For transplants: aerosol ribavirin...probably
 - Toxicity: bronchospasm
- Metapneumovirus
 - None
- Influenza
 - Subject to change, so difficult for board exam
 - Current (2013)
 - All except seasonal H1N1: oral oseltamivir
 - Don't be confused: most common current cause is epidemic H1N1 which is treated with oseltamivir
 - Seasonal H3N2:oral amantadine/rimantadine

Choice of Drug

- Oseltamivir
 - First choice for most cases, including pregnancy UNLESS THERE IS SEASONAL H1N1 (in distinction to the “new strain”)
- Zanamivir
 - Inhalational and available IV on protocol
 - Active against oseltamivir resistant viruses
- Intubated patients
 - Nebulized zanamivir has been associated with respiratory failure and death
 - IV zanamivir or IV Peramivir are available on protocols

Principles of Mechanical Ventilation I

Design Features and Mechanics

Neil MacIntyre MD
Duke University Medical Center
Durham NC

Principles of Mechanical Ventilation

- Design features
 - Breath design
 - Modes
- Respiratory system mechanics
 - Pressure/flow/volume

Design features



1530-Bellows Method

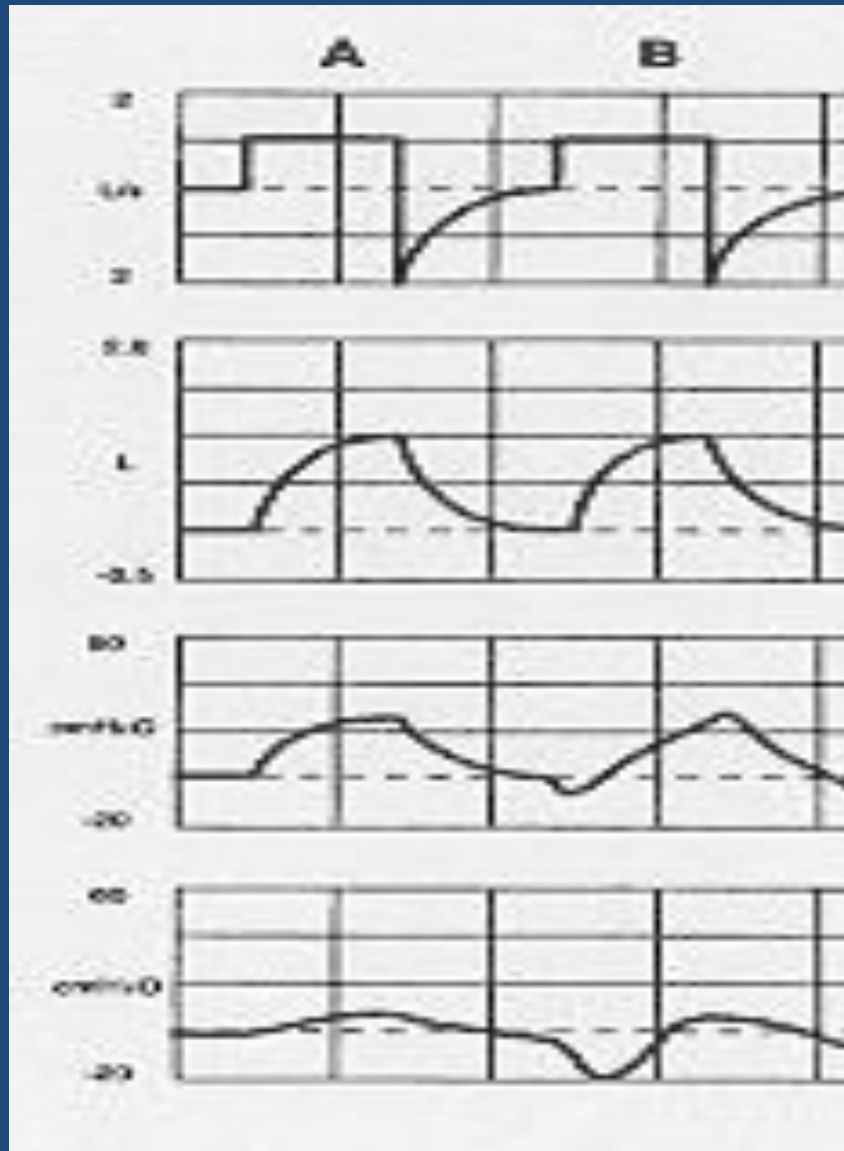
Fireplace bellows first used by the Swiss physician Paracelsus to introduce air into lungs. Variations used in Europe for 300 years.

Question:

- A ventilator pbreath that is patient triggered, pressure targeted, and time cycled is:
 - A. A volume control breath
 - B. A volume assist breath
 - C. A pressure controlled breath
 - D. A pressure assist breath
 - E. A pressure support breath

Breath characteristics

- Trigger
 - what initiates breath
 - timer (control) vs effort (assist)
- Gas delivery target or limit
 - what governs gas flow
 - set flow vs set insp pressure
- Cycle
 - what terminates the breath
 - volume, time, flow, pressure



Flow

Vol

Paw

Pes

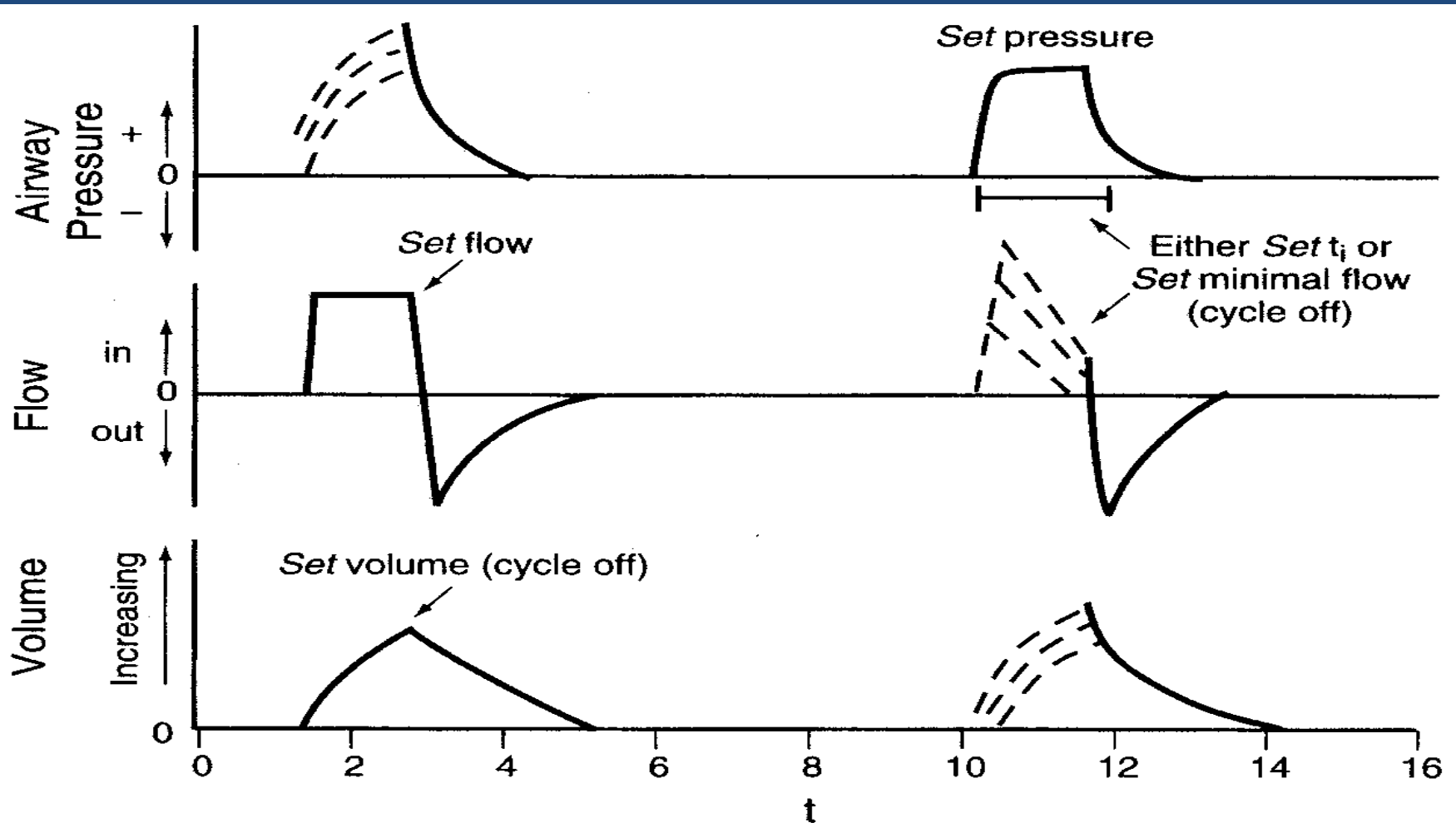
Breath characteristics

Trigger

- Controlled - machine timer
 - Assisted/supported - patient effort
 - Pressure trigger - effort produces pressure drop in vent circuit
 - sensitivity determined by set pressure drop
 - Flow trigger - effort draws gas out of a continuous flow through the vent circuit
 - sensitivity determined by amount of flow taken by patient
- * some vents have both and trigger off the first detected

Breath characteristics

Gas Delivery



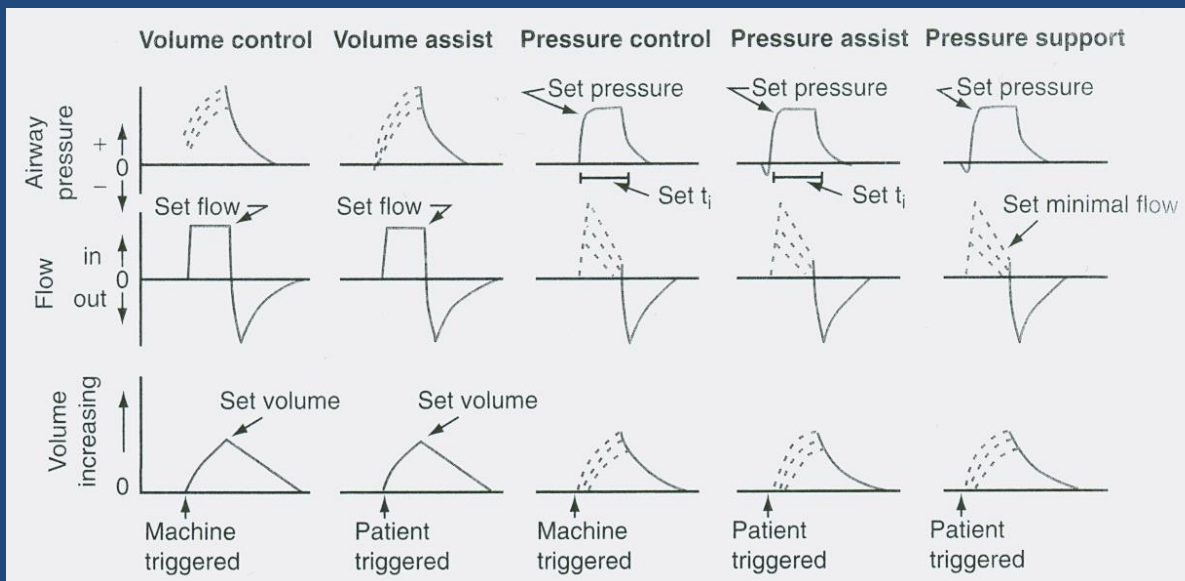
Breath characteristics

Cycle

- Three common types
 - reach set volume
 - reach set time
 - reach certain flow reduction
- Airway pressure as “backup” cycle
 - pressure alarm and cycle with occlusions or expiratory efforts

Breath characteristics

	TRIGGER	TARGET/LIMIT	CYCLE
Volume control (VC) _____	time	flow	vol*
Volume assist (VA) _____	effort	flow	vol*
Pressure control (PC) _____	time	Pi**	time*
Pressure assist (PA) _____	effort	Pi**	time*
Pressure support (PS) _____	effort	Pi**	flow*



Modes of support

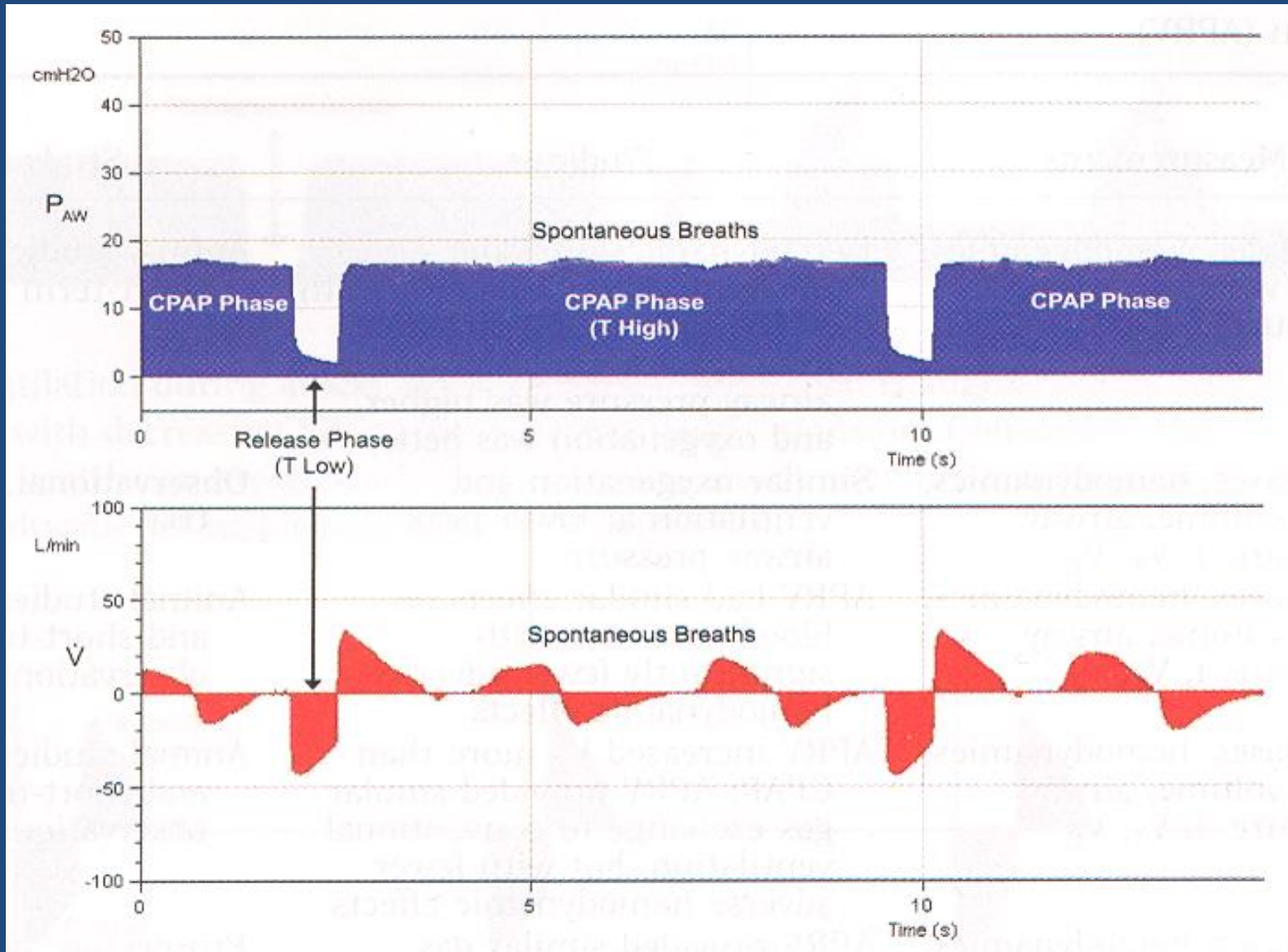
BREATHS TYPES AVAILABLE

VC VA PC PA PS SP

MODES

Volume Assist Control	x ^{1,2}	x				
Pressure Assist Control			x ^{1,2,3}	x ³		
Volume SIMV	x	x			x ¹	x
Pressure SIMV			x	x	x ¹	x
PSV					x ¹	

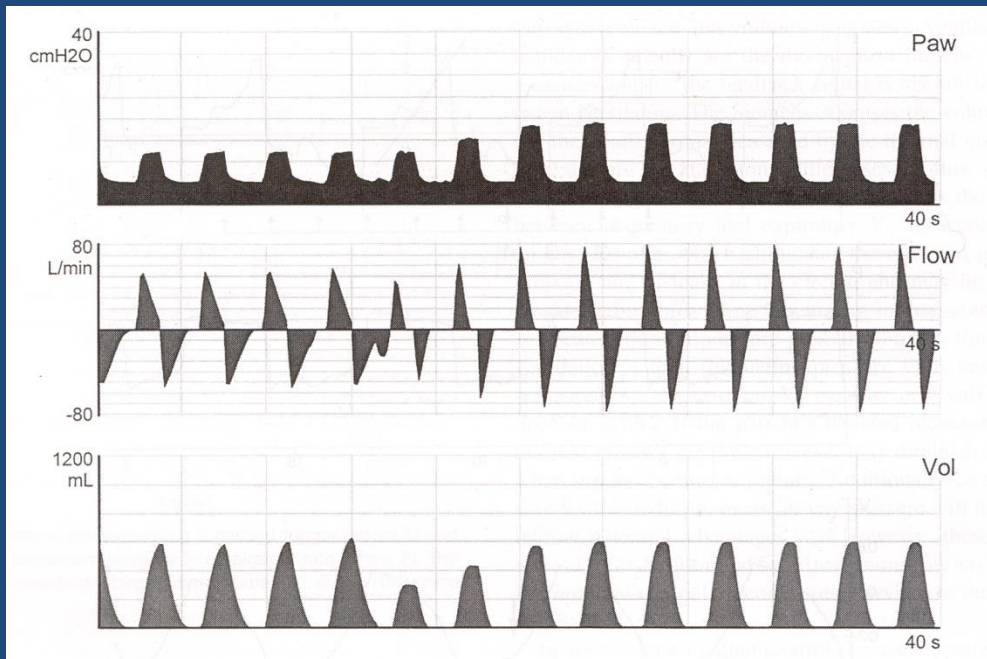
APRV: pressure target/spont breaths



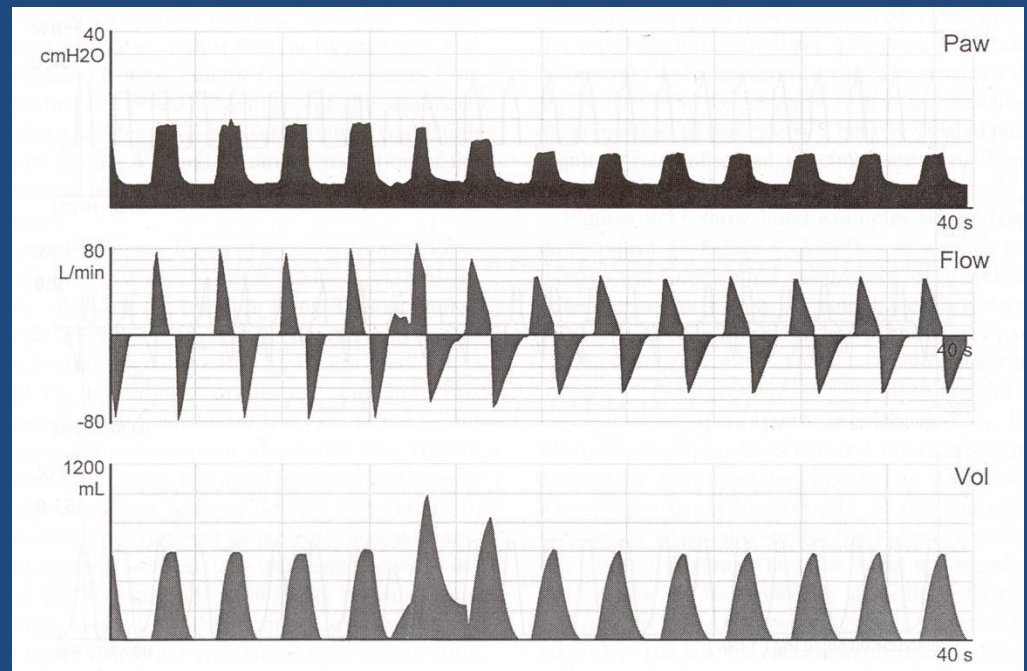
Feedback Control

- Feedback of pressure targeted breaths
 - VT: PRVC-VS
 - Adaptive support (ASV)
- New interactive strategies
 - PAV
 - NAVA

Response to reduced compliance



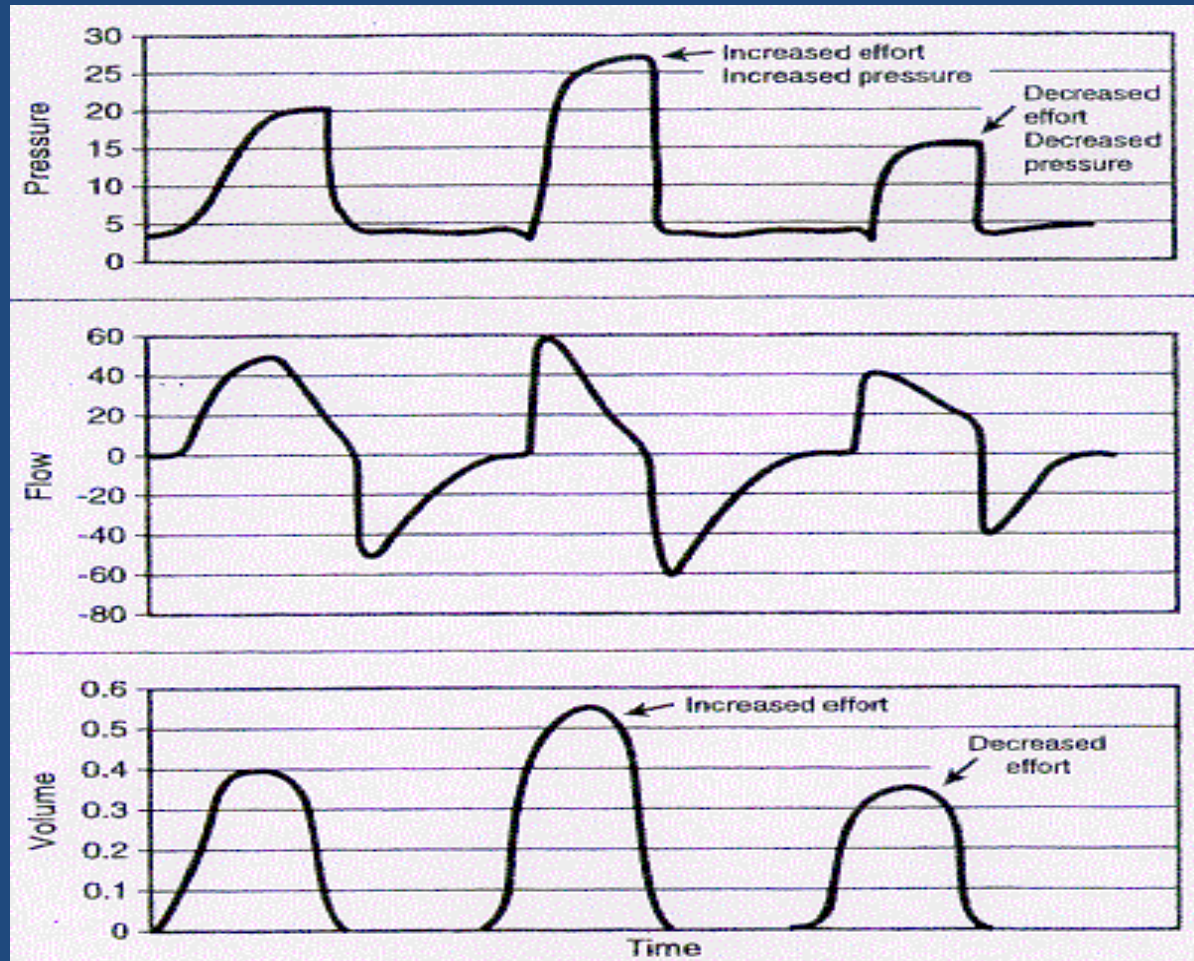
Response to improved compliance

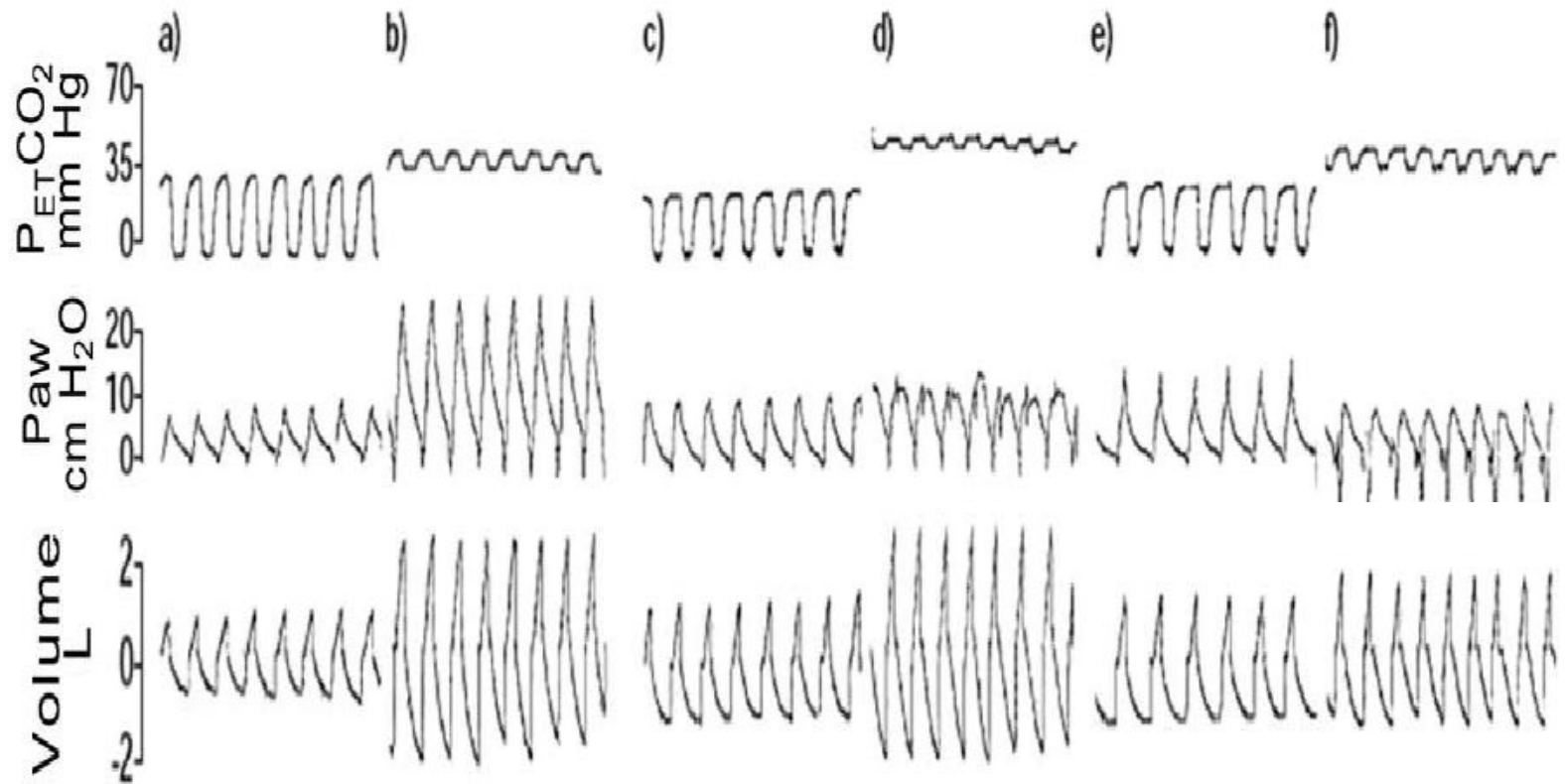


Feedback Control

- Feedback of pressure targeted breaths
 - VT: PRVC-VS
 - Adaptive support (ASV)
- New interactive strategies
 - PAV
 - NAVA

Proportional Assist Ventilation (PAV)





PAV

PSV

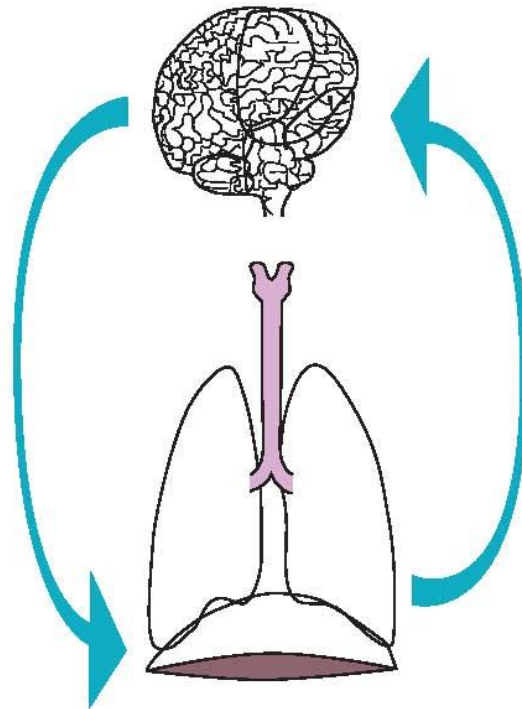
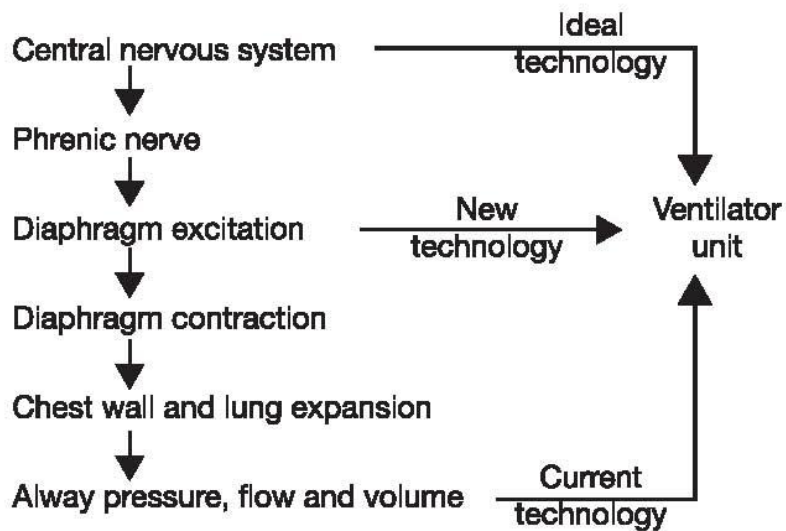
VACV

PAV – Clinical Application

- Performs as designed - gives comfortable support
 - *Int Care Med 2008 on line*
 - *Thorax 2002;57:79*
 - *J Appl Physiol 1996;81:429*
 - *Am J Resp Crit Care Med 1996;153:1005*
- No good outcomes trials to date
- Reasonable to use in pts with flow or cycle dys-synchrony
 - Will still have triggering (incl PEEPi) issues
 - Will require monitors/alarms for low, unstable drive

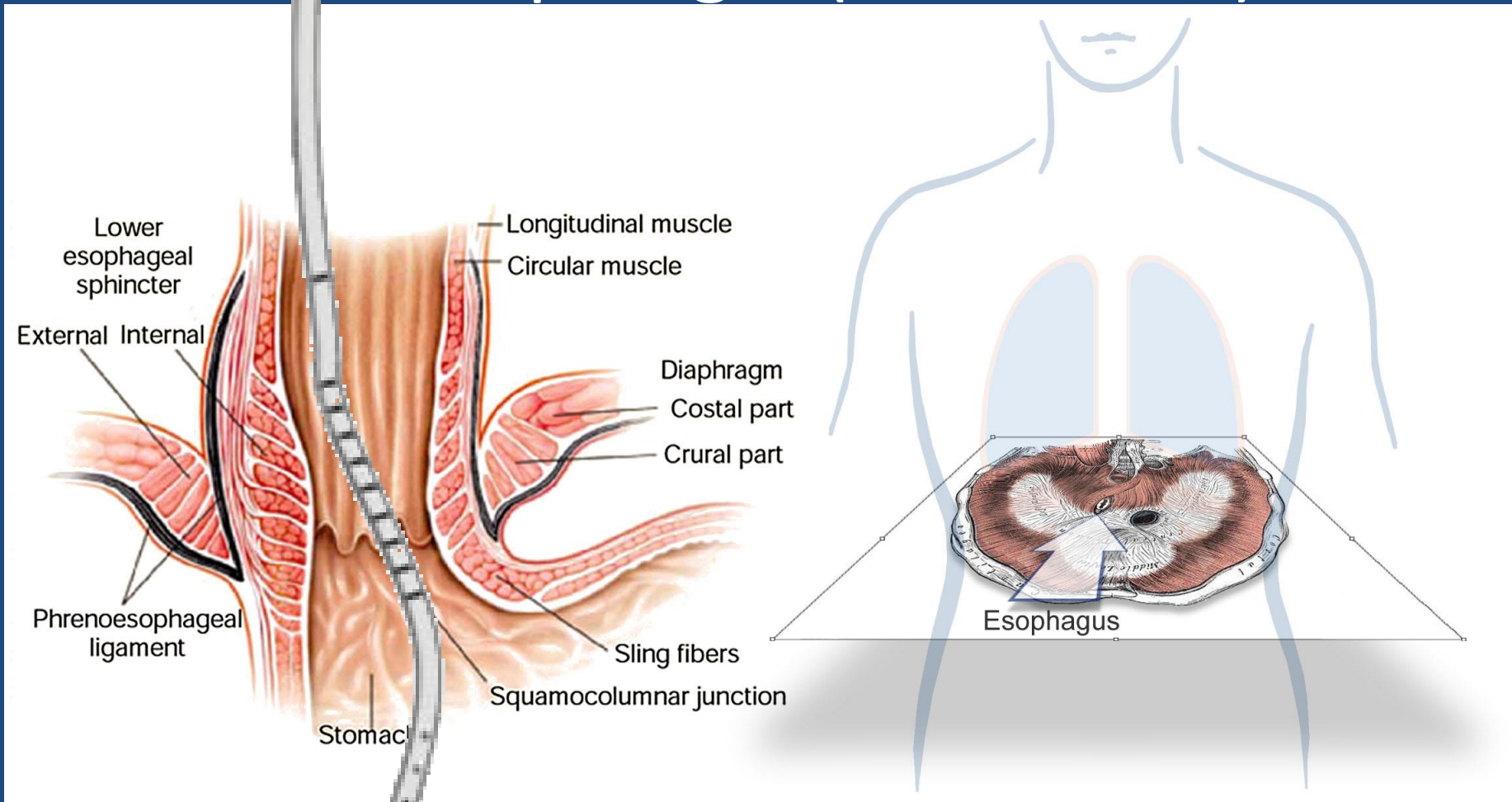
NAVA concept

Neuro-ventilatory coupling



Nature 1999

Catheter for measuring electrical activity of the diaphragm (EAdi or Edi)

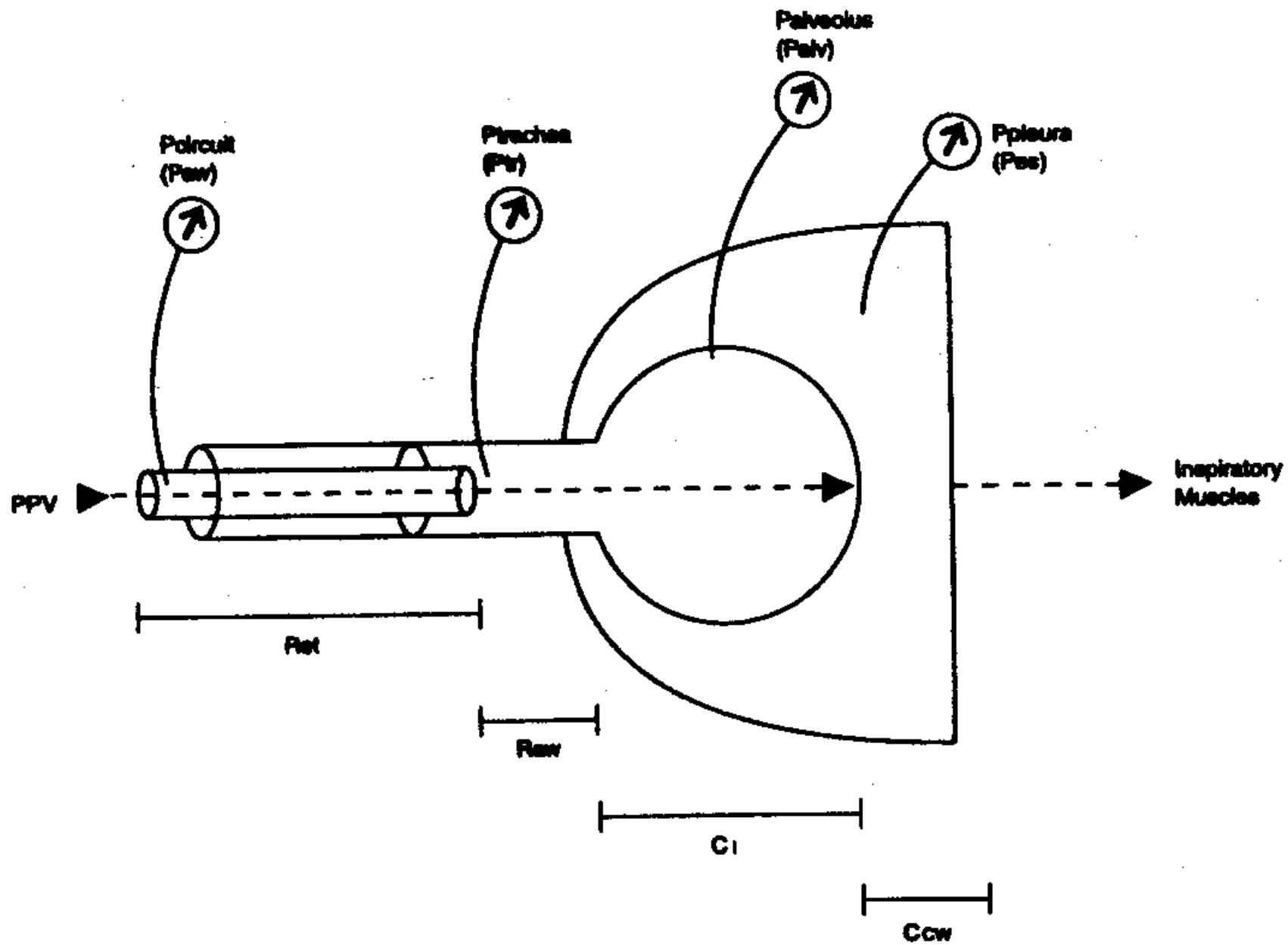


NAVA – Clinical Application

- Performs as designed
 - *Intensive Care Med.* 2010 Sep 25.
 - *Anesthesiology.* 2010;113:925
 - *Crit Care Med.* 2010;38:518
- No good outcomes trials to date
- Theoretically attractive BUT:
 - Catheters expensive and invasive
 - Needs dedicated control system (also expensive)
 - Like PAV_< will require monitors/alarms for low, unstable drive

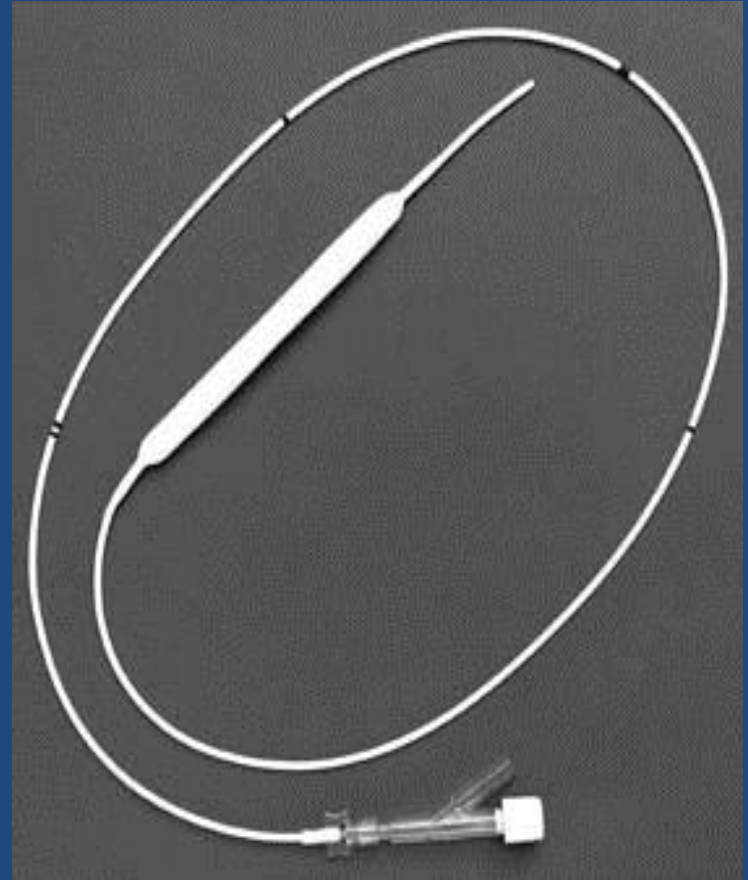
Principles of Mechanical Ventilation

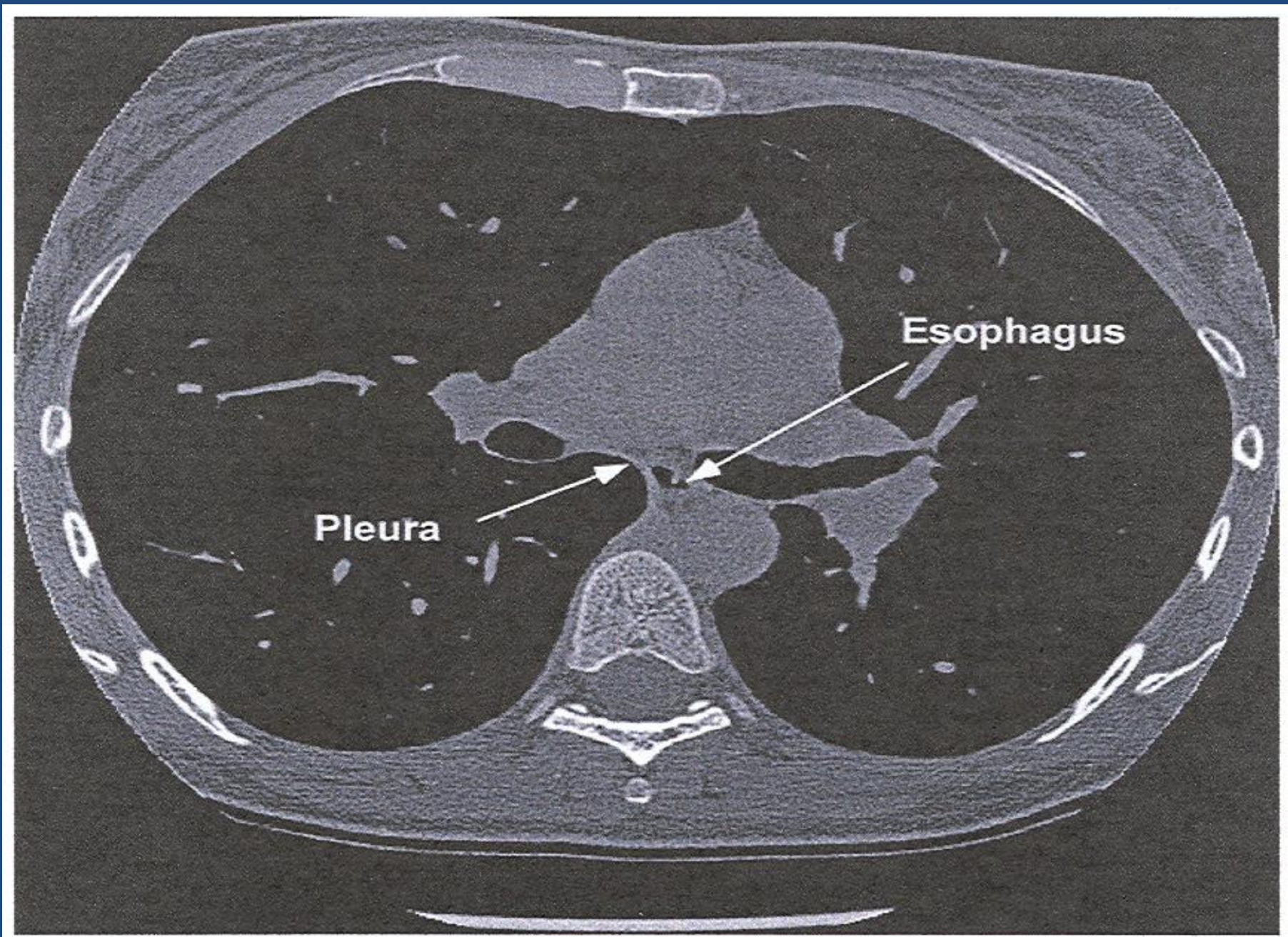
- Design features
 - Breath design
 - Modes
- Respiratory system mechanics
 - Pressure/flow/volume



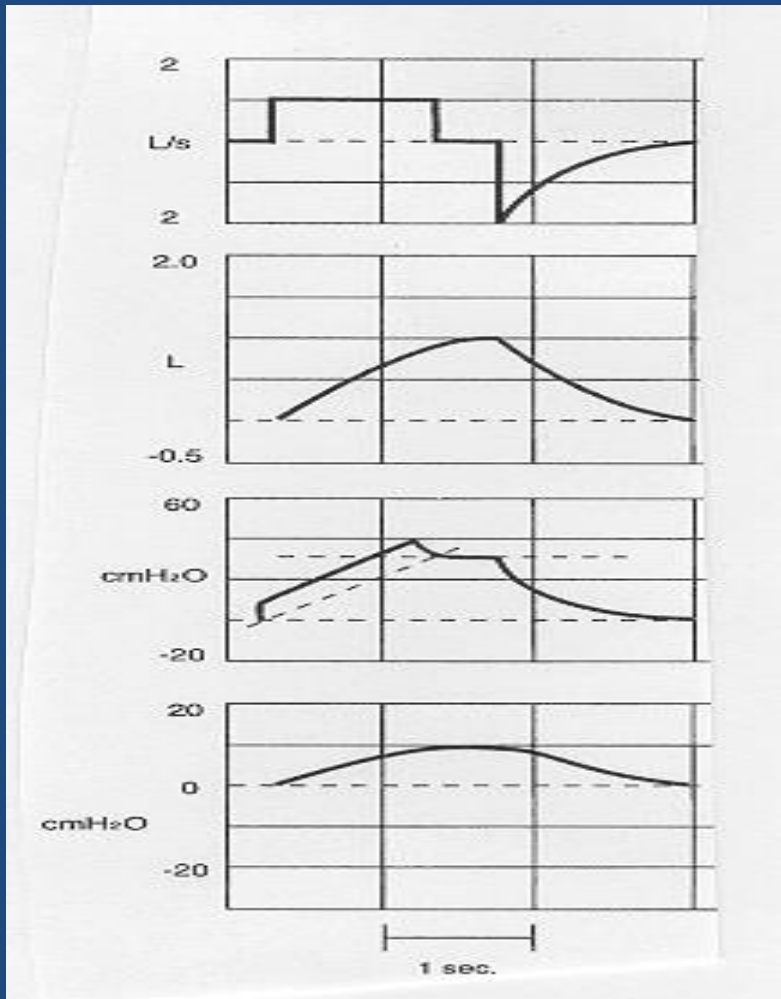
Esophageal Balloon

- Approximates pleural pressure
- Polyethylene
- 10 cm long balloon
- 100 cm long tubing
- Positioned in the lower 1/3 of the esophagus
- Filled with 0.5-1.0cc air





Mechanical effects of PPV



Insp flow = 1 L/sec
Exp flow (peak) = 2 L/sec

V_t = 1 Liter

Peak P = 40 cm H₂O

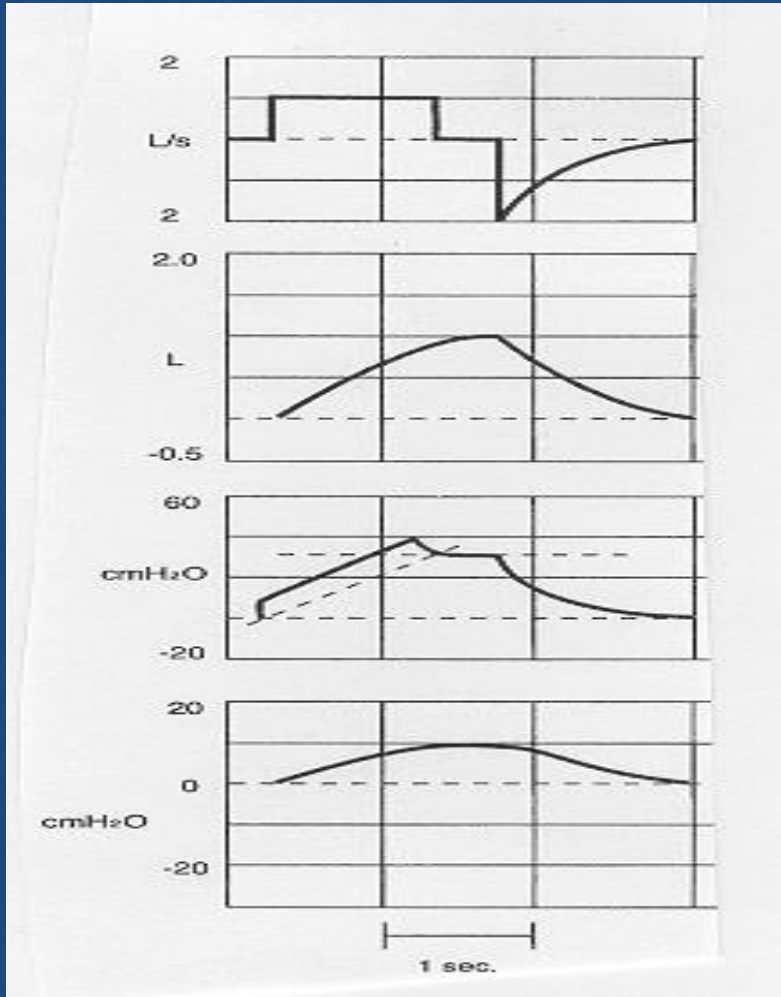
Plat P = 30 cm H₂O

Base P (PEEP) = 0 cm H₂O

Peak P_{es} = 10 cm H₂O

Base P_{es} = 0 cm H₂O

Mechanical effects of PPV

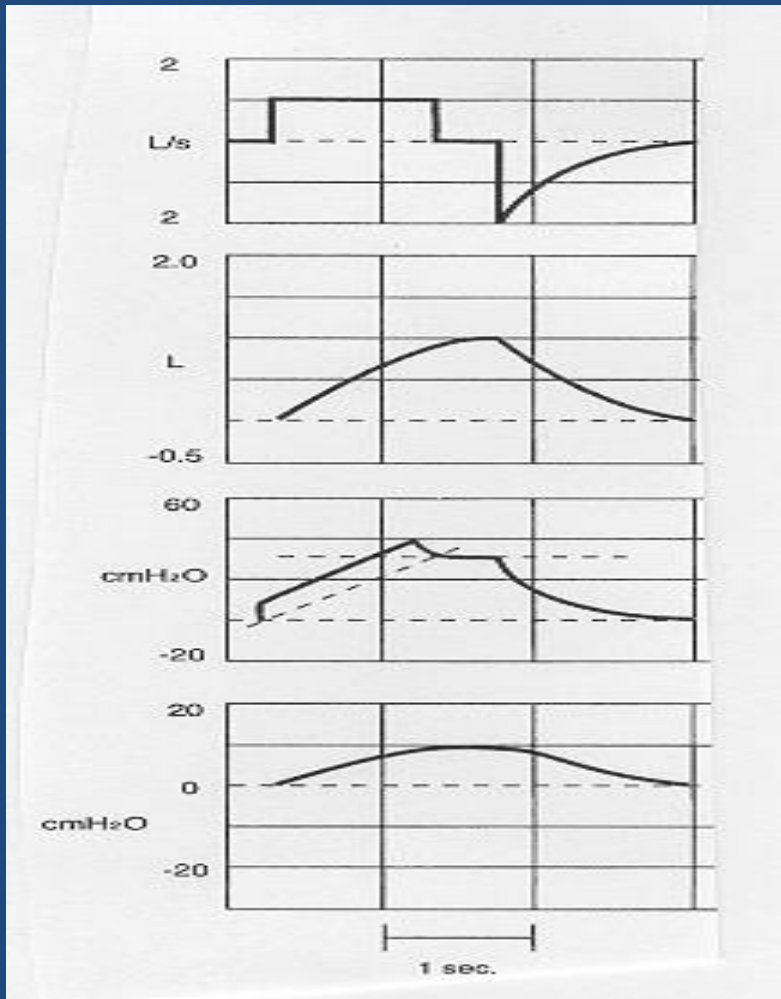


FLOW PRESSURES ($P = V' \times R$):

Peak P - PlatP = pressure for flow
 $= 40 - 30 = 10 \text{ cm H}_2\text{O}$

Resistance = $P/V' = 10/1 = 10 \text{ cm/l/s}$

Mechanical effects of PPV



DISTENDING PRESSURES ($P=V/C$):

Plat P - Base P (PEEP) = pressure
to distend resp system
(lung plus CW) = $30-0=30$

PeakPes - BasePes = pressure to
distend CW = $10-0=10$

PlatP - BaseP(PEEP) - PeakPes -
BasePes = pressure to
distend lungs =
 $30-0-10-0=20$

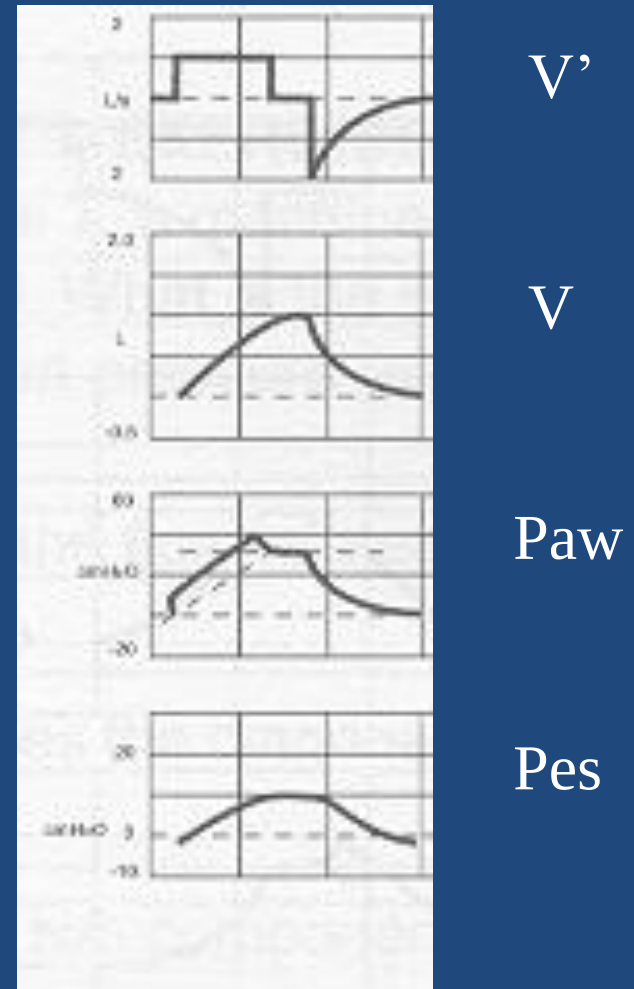
$$C_{rs} = V/P_{rs} = 1000/30 = 33 \text{ ml/cm}$$

$$C_{cw} = V/P_{cw} = 1000/10 = 100 \text{ ml/cm}$$

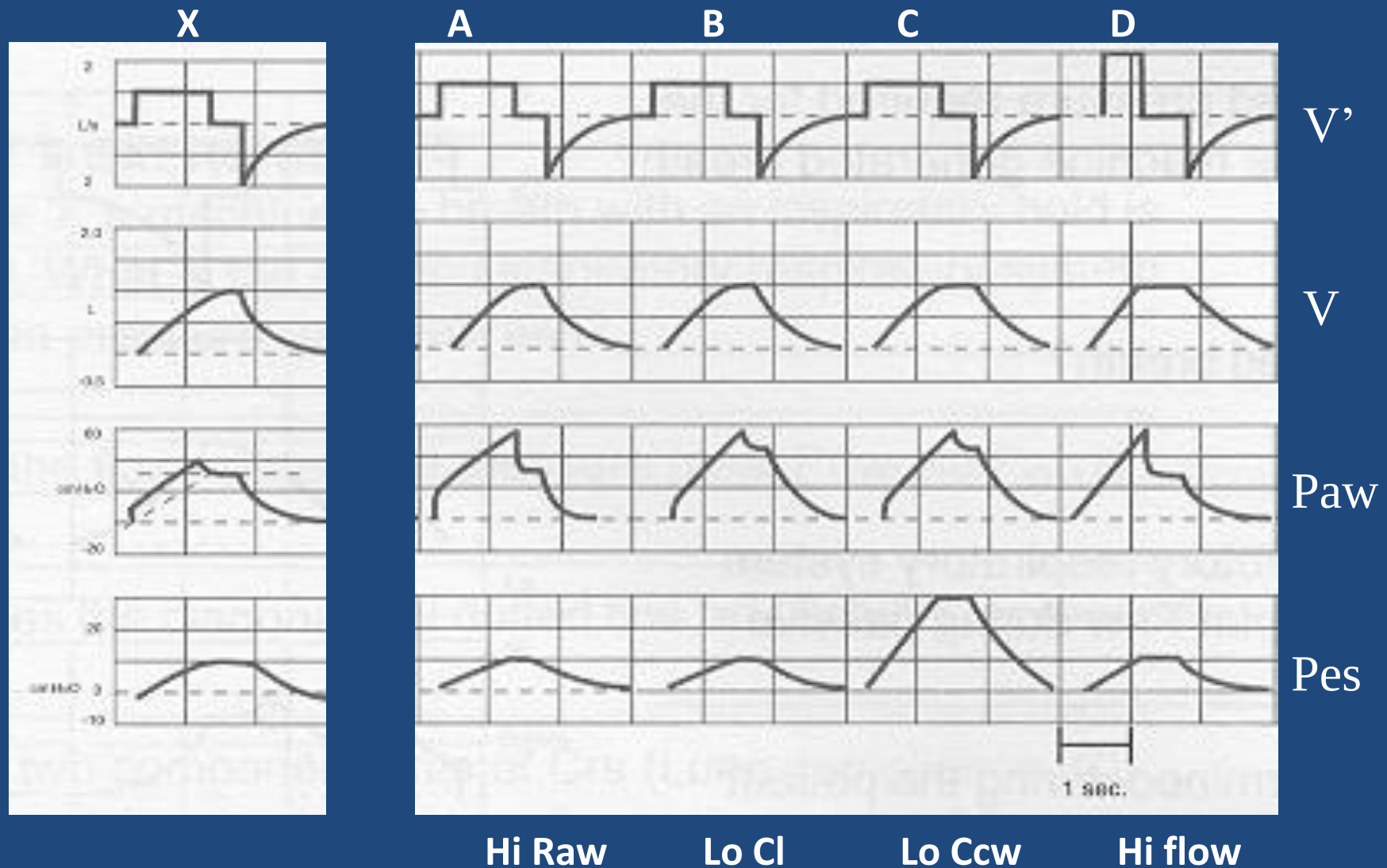
$$C_l = V/P_l = 1000/20 = 50 \text{ ml/cm}$$

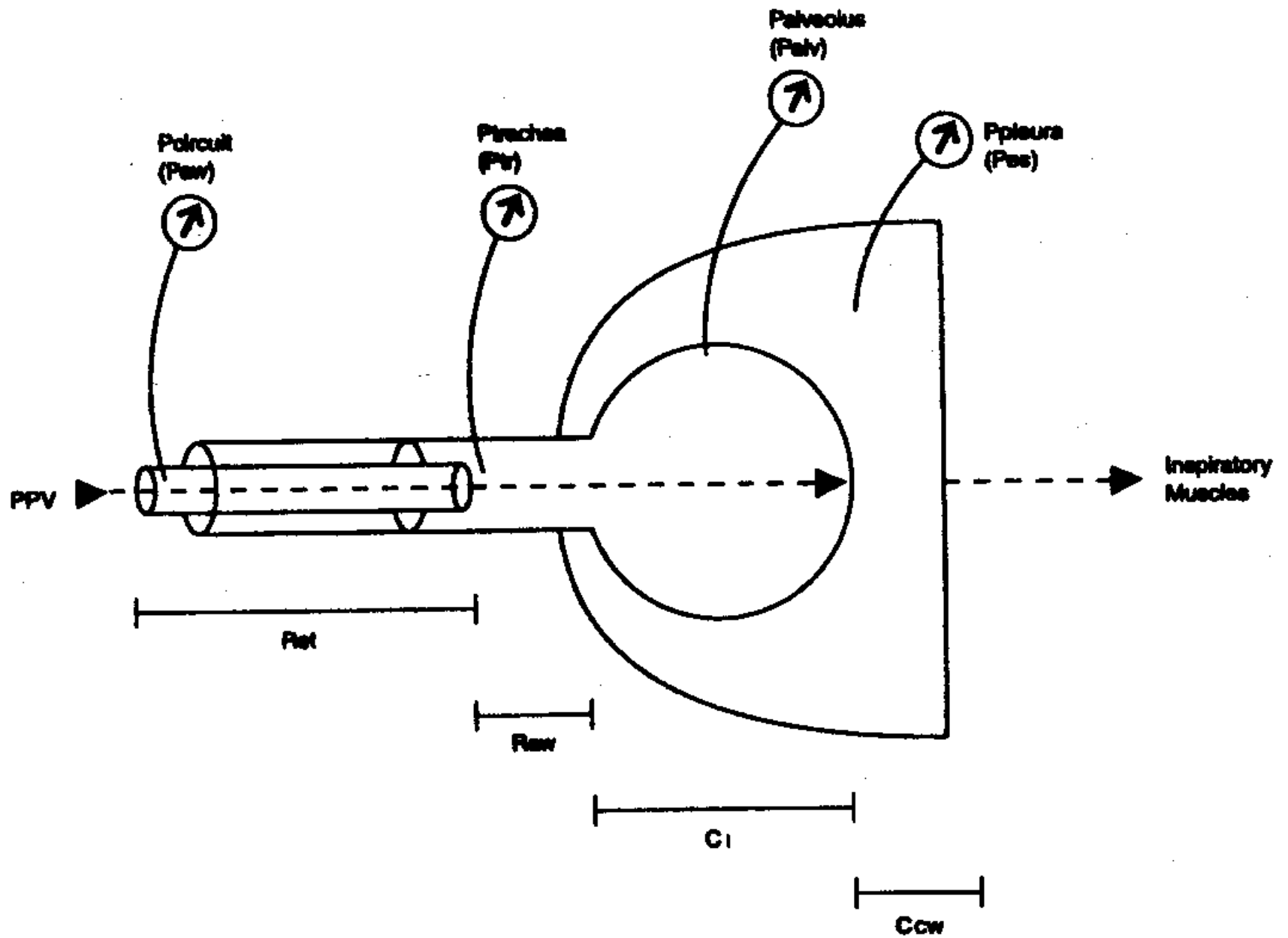
Case:

A 55 yo woman is receiving mechanical ventilation with volume assist-control. Her baseline ventilator graphics are displayed. Six hours later she develops acute pulmonary edema on CXR and obvious rales are present on exam. The peak pressures on the ventilator also go up and alarms are activated.

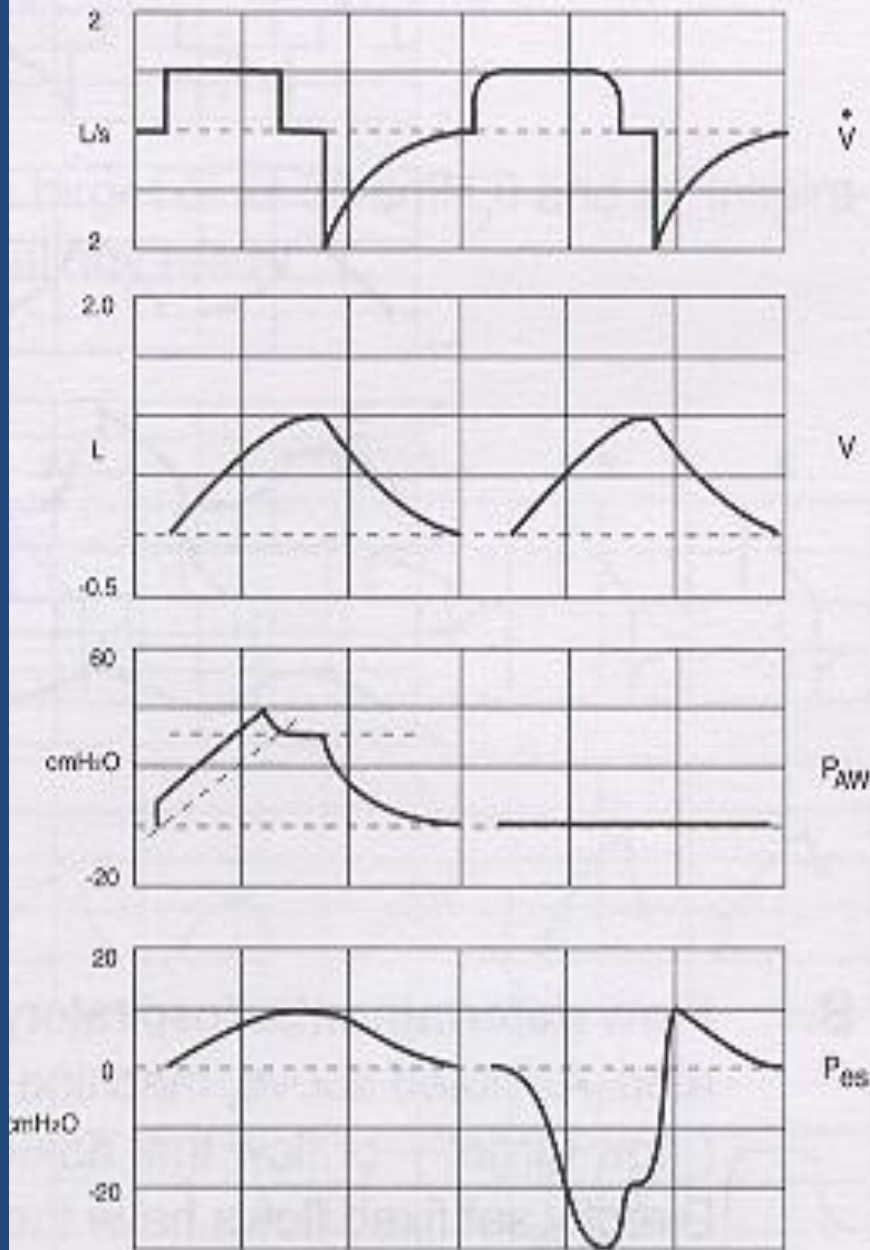


Question: Breath X is baseline. Breaths A-D all have elevated Peak P. Which change is most consistent with acute pulm edema ?





During patient generated breaths, P_{es} is now the driving pressure “pulling” the lung open. With similar flows and an end insp pause, the same mechanics calculations can be done.



Principles of Mechanical Ventilation

- Design features
 - Breath design
 - Modes
- Respiratory system mechanics
 - Pressure/flow/volume

Principles of Mechanical Ventilation II

Clinical Challenges

Neil MacIntyre MD
Duke University Medical Center
Durham NC

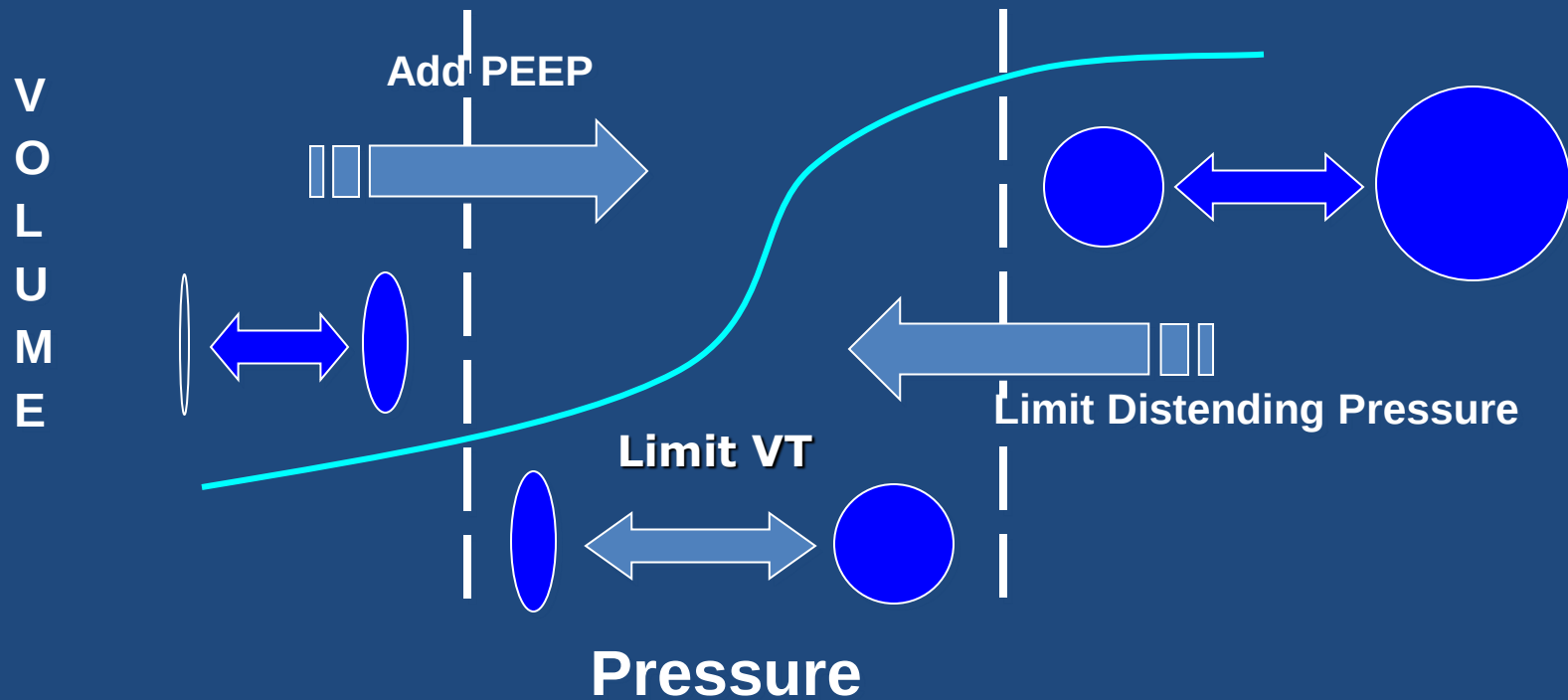
Mechanical Ventilation:

Clinical Challenges

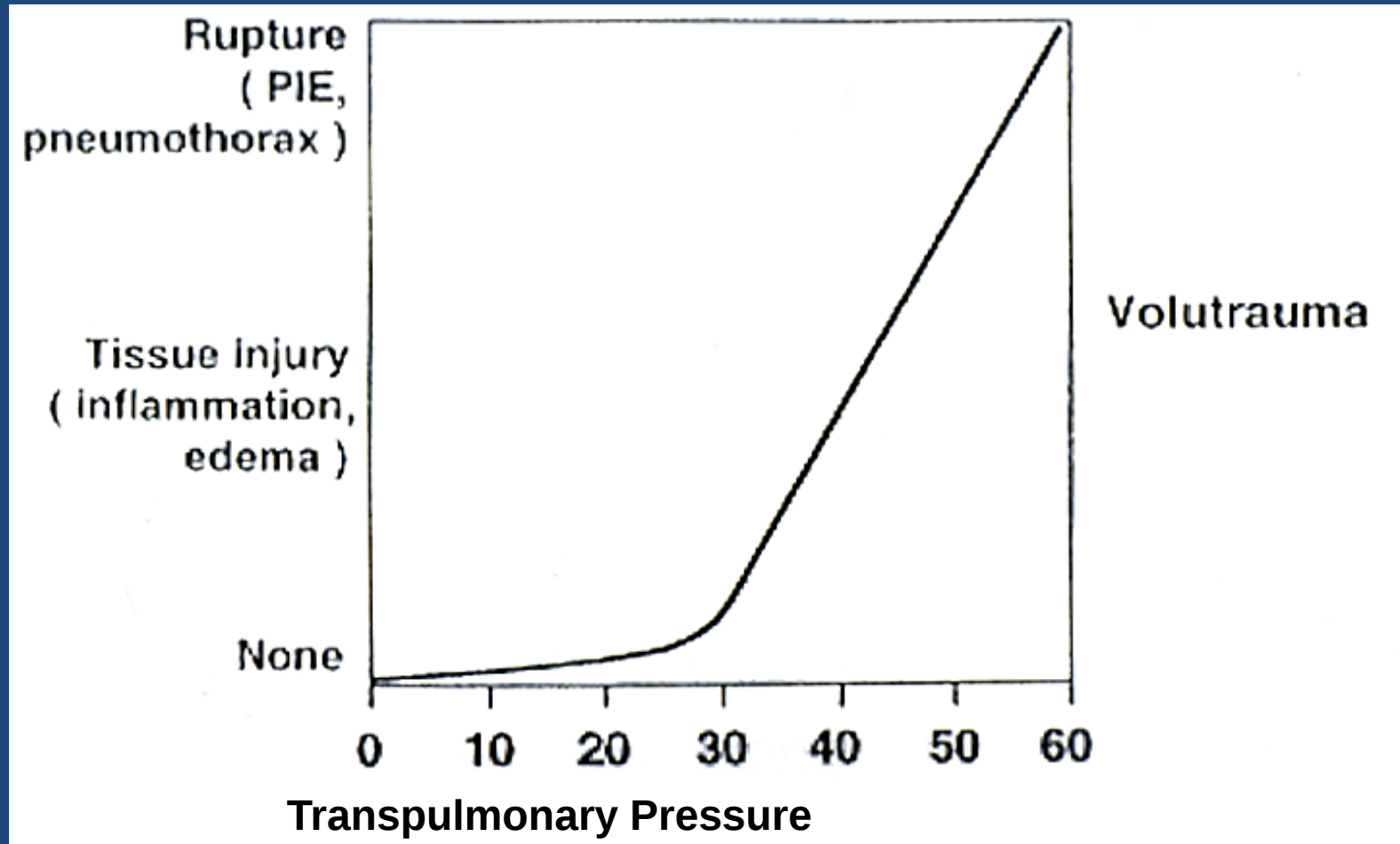
- Lung protection
- Intrinsic PEEP
- Patient ventilator synchrony
- Maintaining cardiac function
- Prompt discontinuation

Preventing Overdistention and Collapse Injury

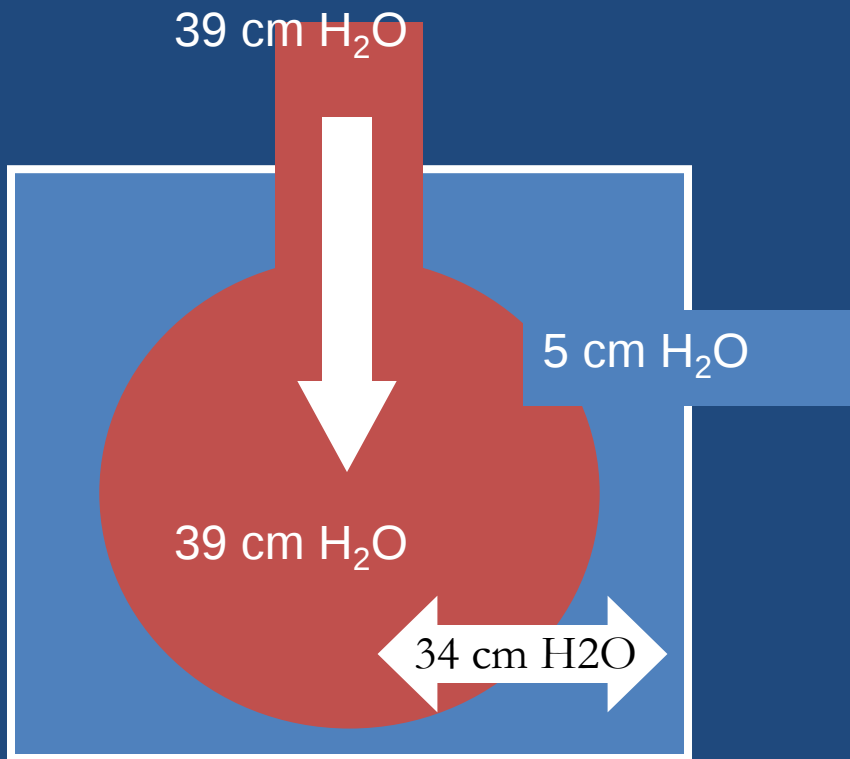
“Lung Protective” Ventilation



Overdistention and VILI

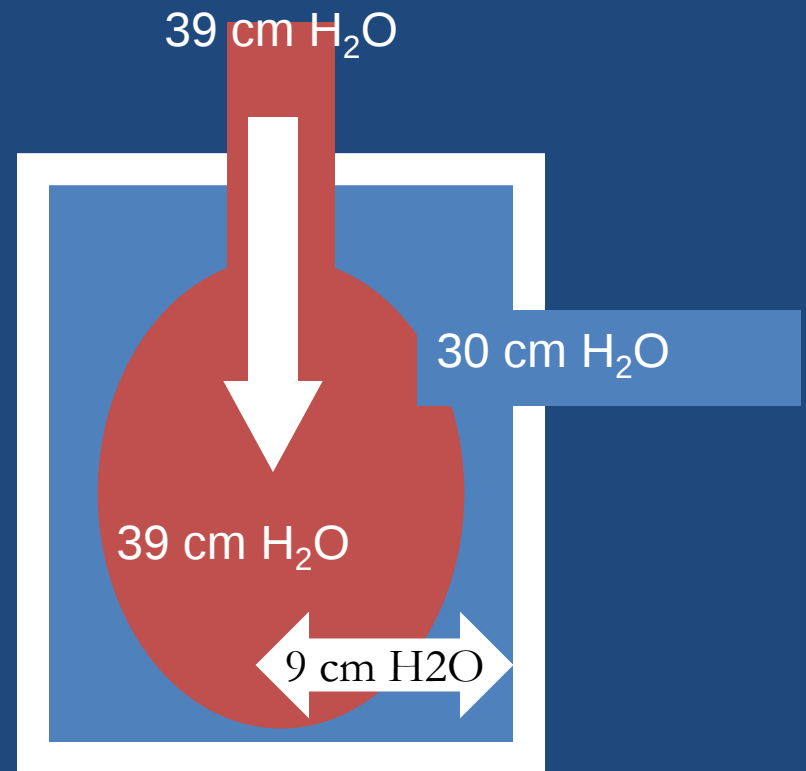
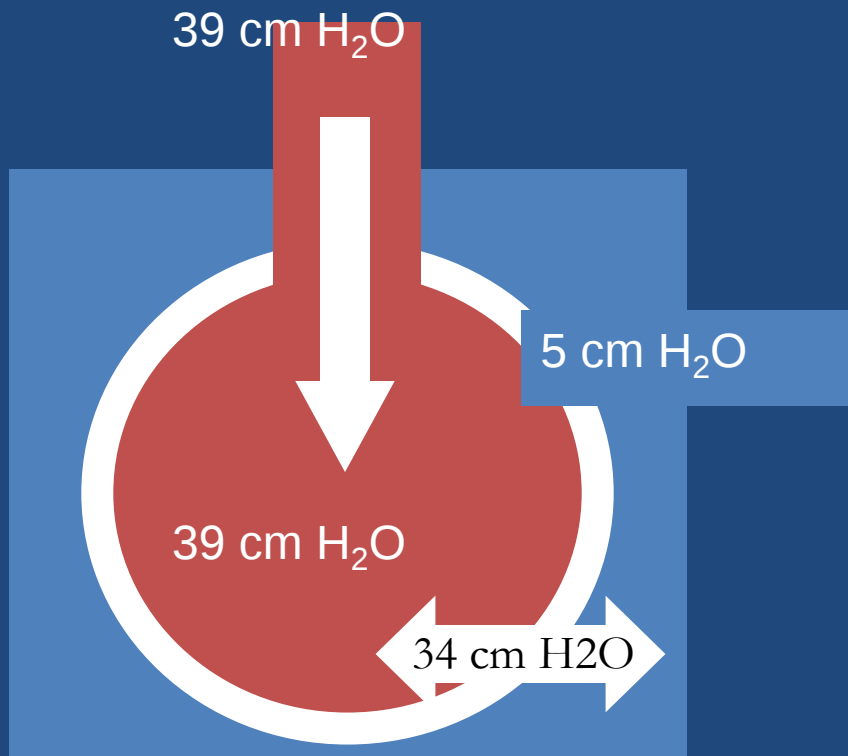


Transpulmonary P = VILI Risk

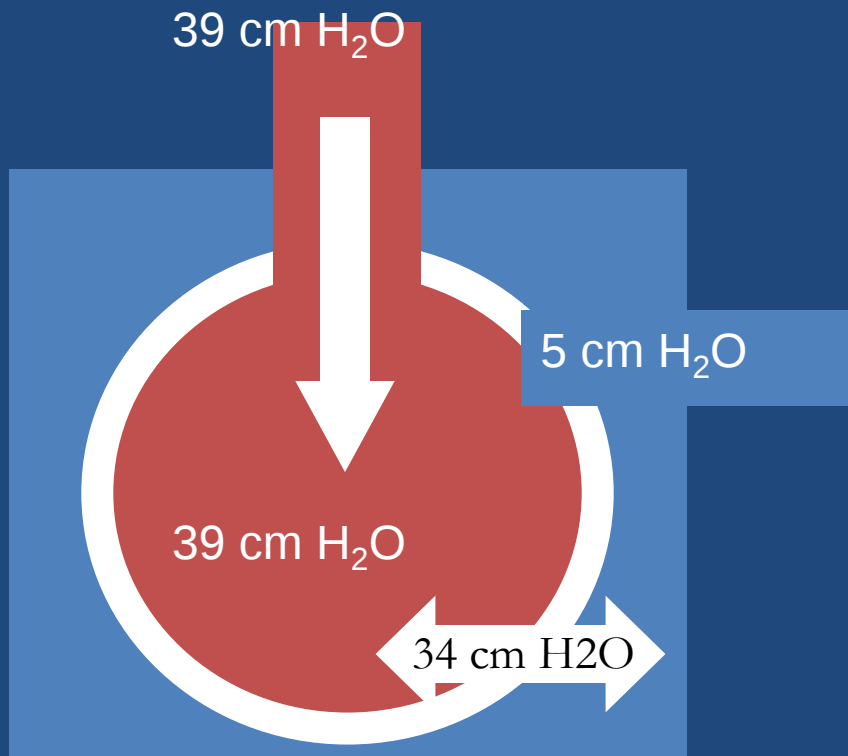


Transpulmonary P:
- P_{plat}-P_{es}
- Distending P

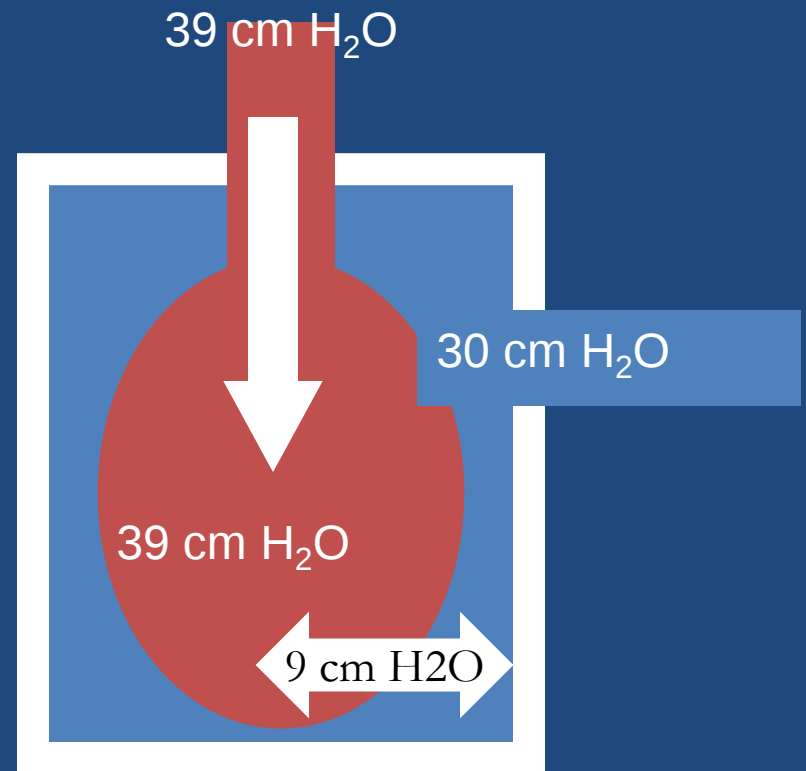
Influence of chest wall stiffness



Influence of chest wall stiffness



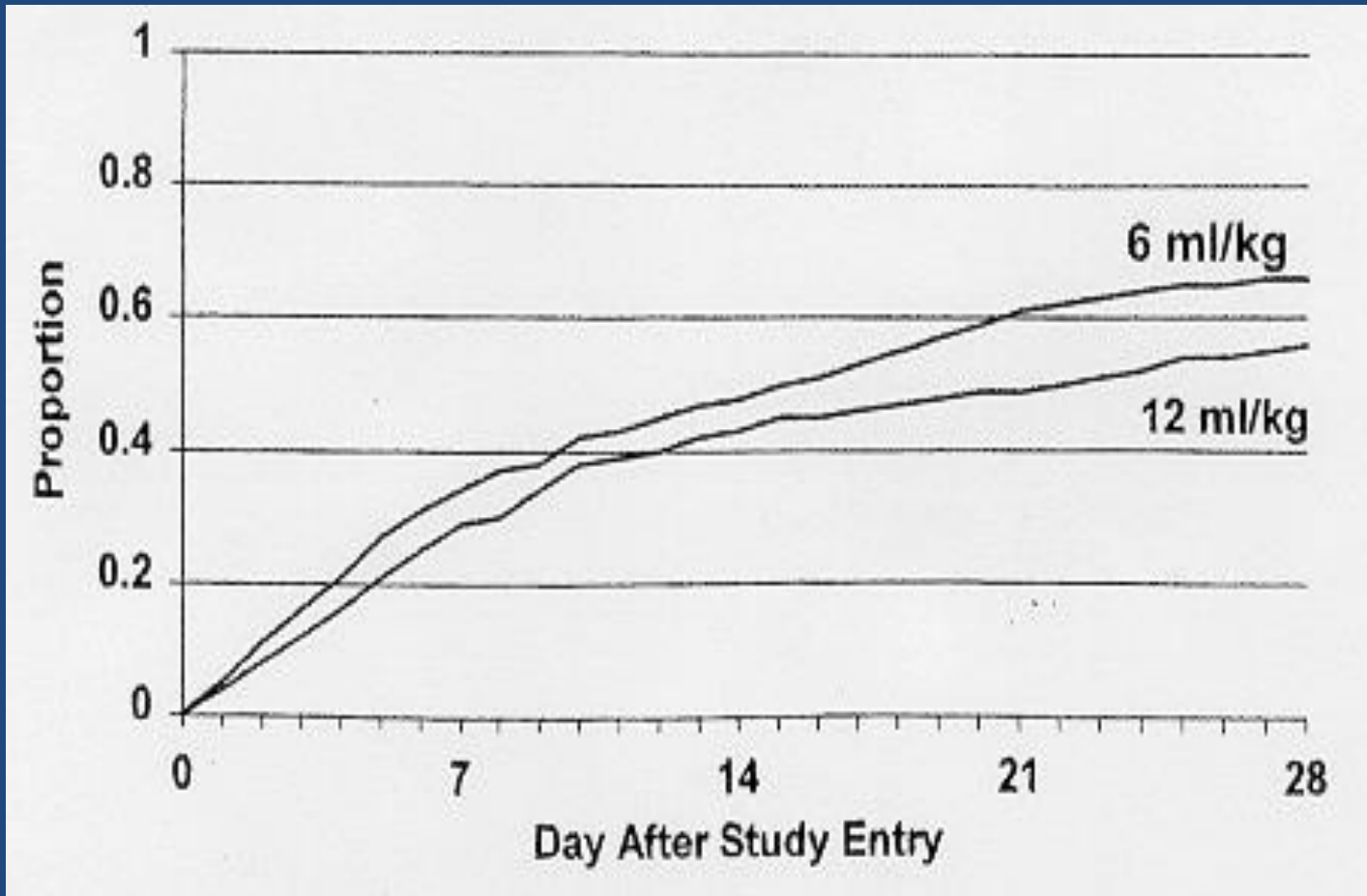
Unsafe to add more P_{aw}



Safe to add more P_{aw}

NIH ARDS Network trial

NEJM 2000;342:1301

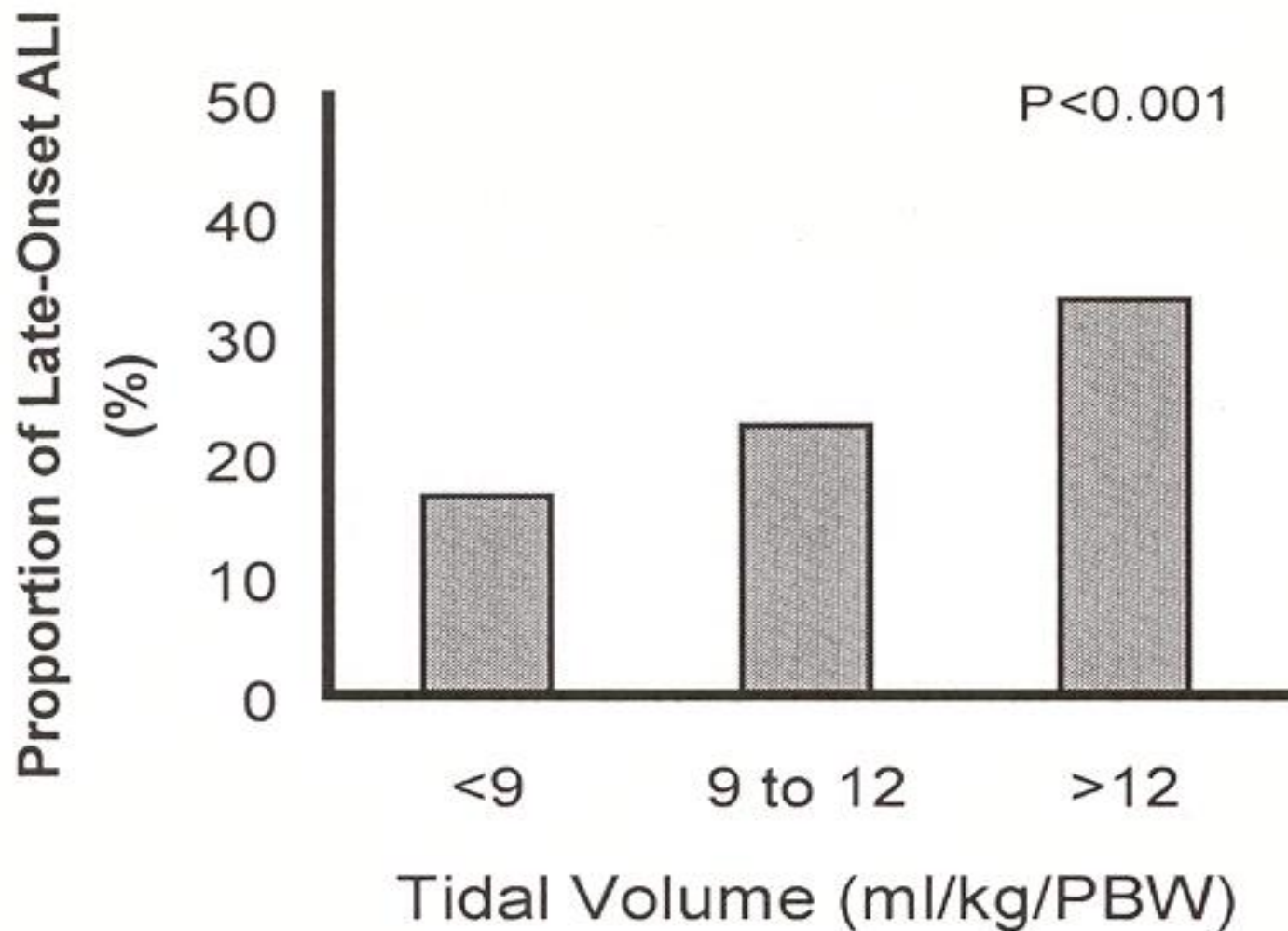


Pplat =

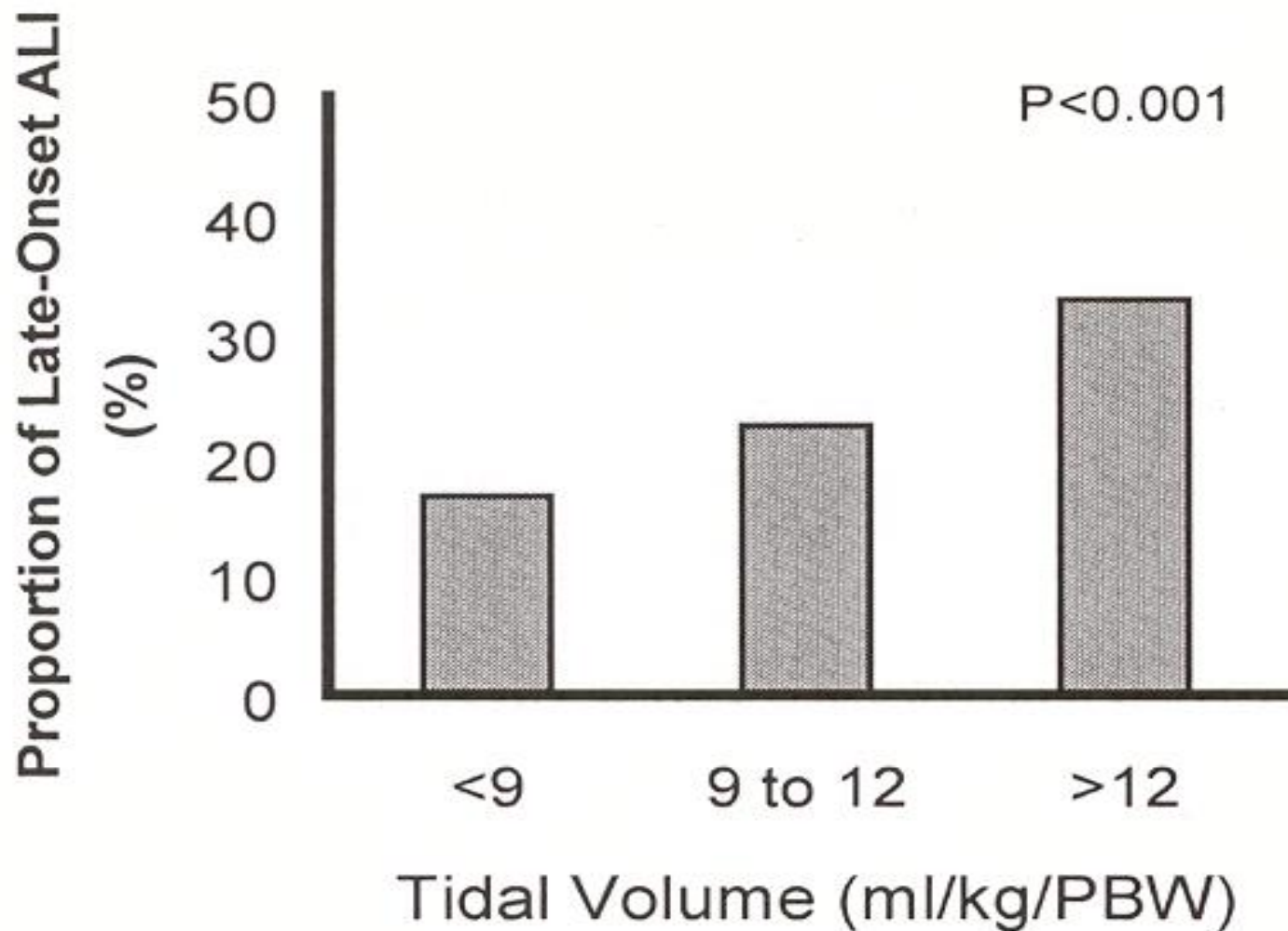
mid 20s
low 30s

Controversies in VILI - Overdistention

- Is it “maximal” stretch or “tidal” stretch (or both) that causes VILI?
 - If “maximal” , goal is to keep Pplat <30 with any VT
 - Pplat < 30 is “safe”
 - If “tidal”, goal is to reduce VT and Pplat to minimums
 - No Pplat is “safe”

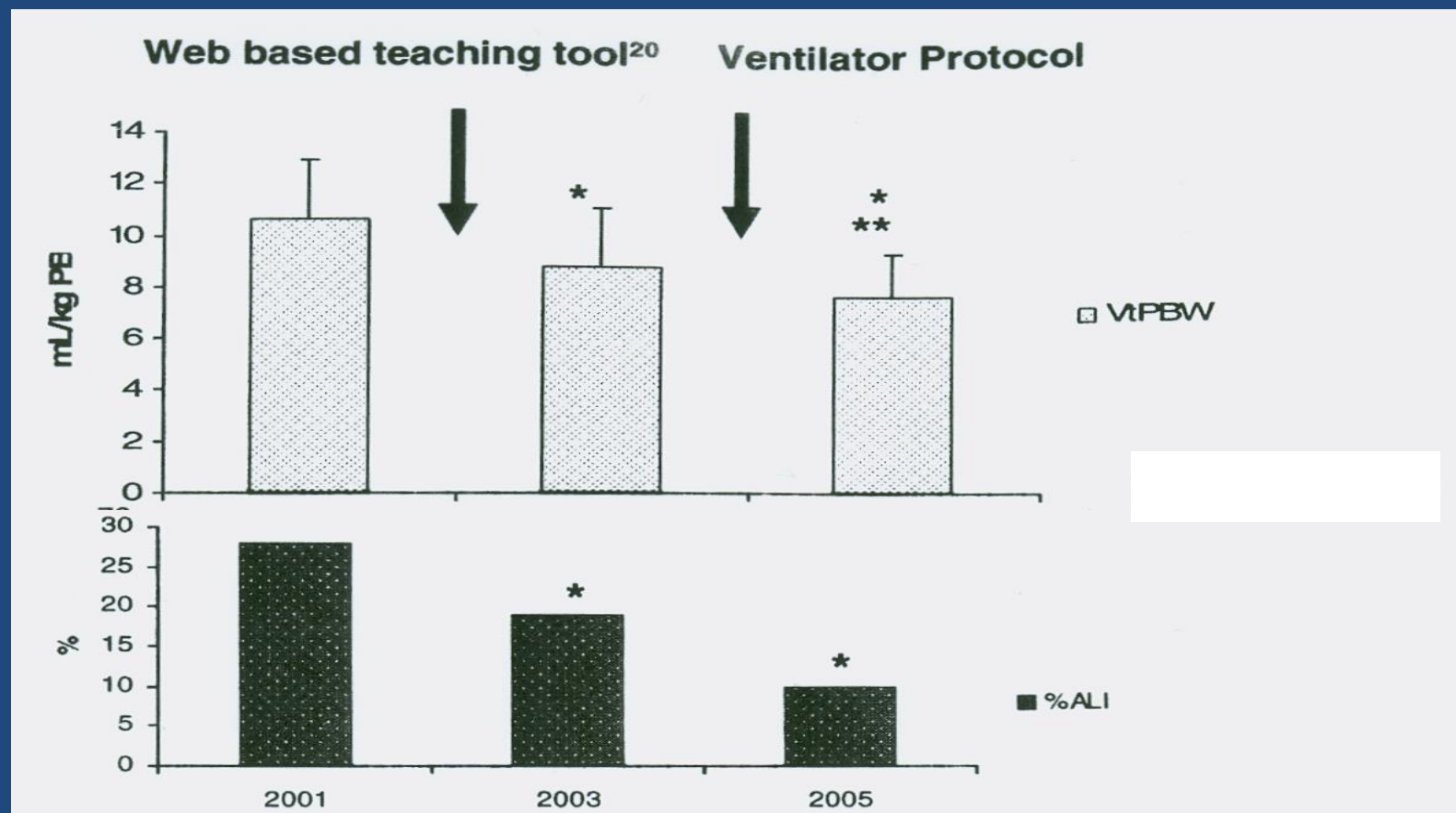


Peak P	35	29	32
Crs	.37	.46	.52
AP III	77	69	69
Post op	38	61	66



Peak P	35	29	32
Crs	<u>.37</u>	<u>.46</u>	<u>.52 (Pplat = 20)</u>
AP III	77	69	69
Post op	<u>38</u>	<u>61</u>	<u>66</u>

Crit Care Med.
2004; 32:1817.



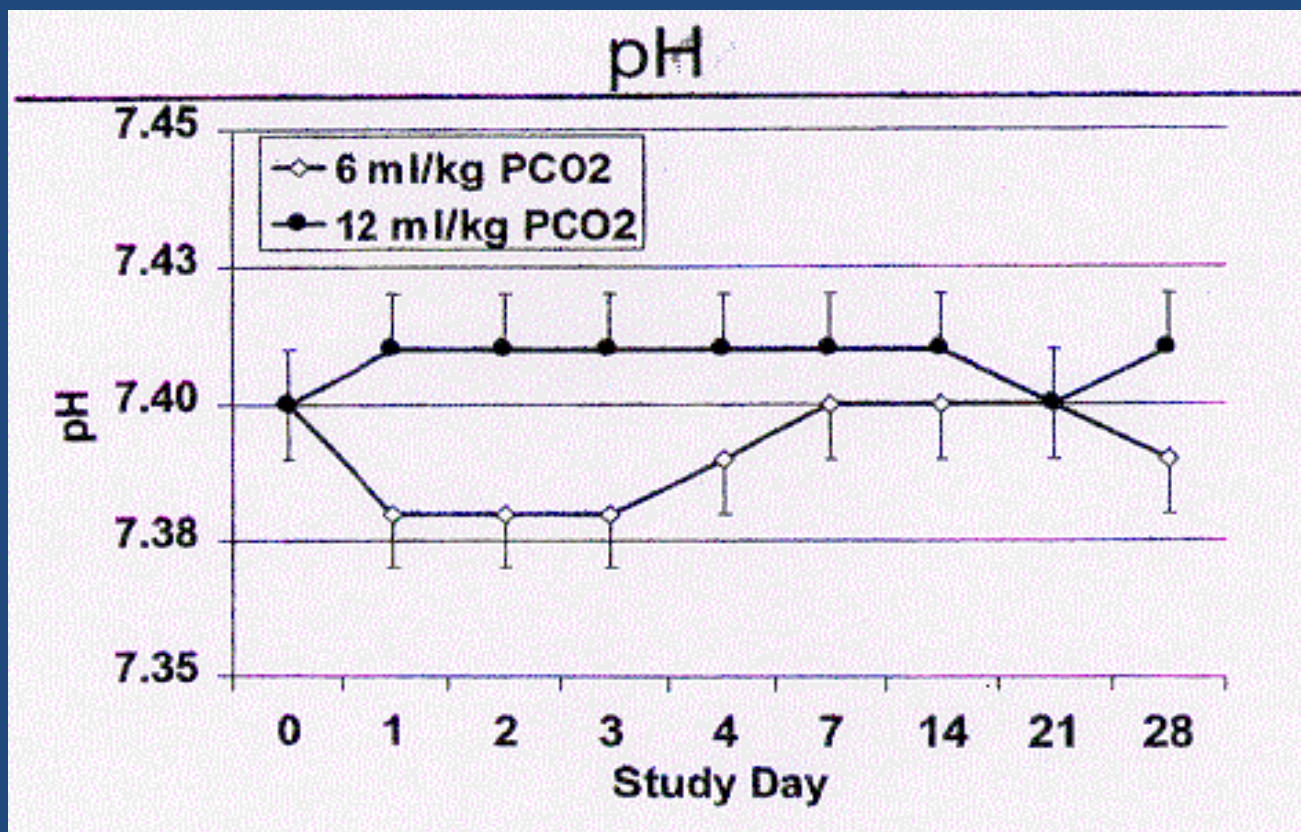
Controversies in VILI - Overdistention

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Controversies in VILI - Overdistention

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Balancing lung protection vs pH and PCO₂

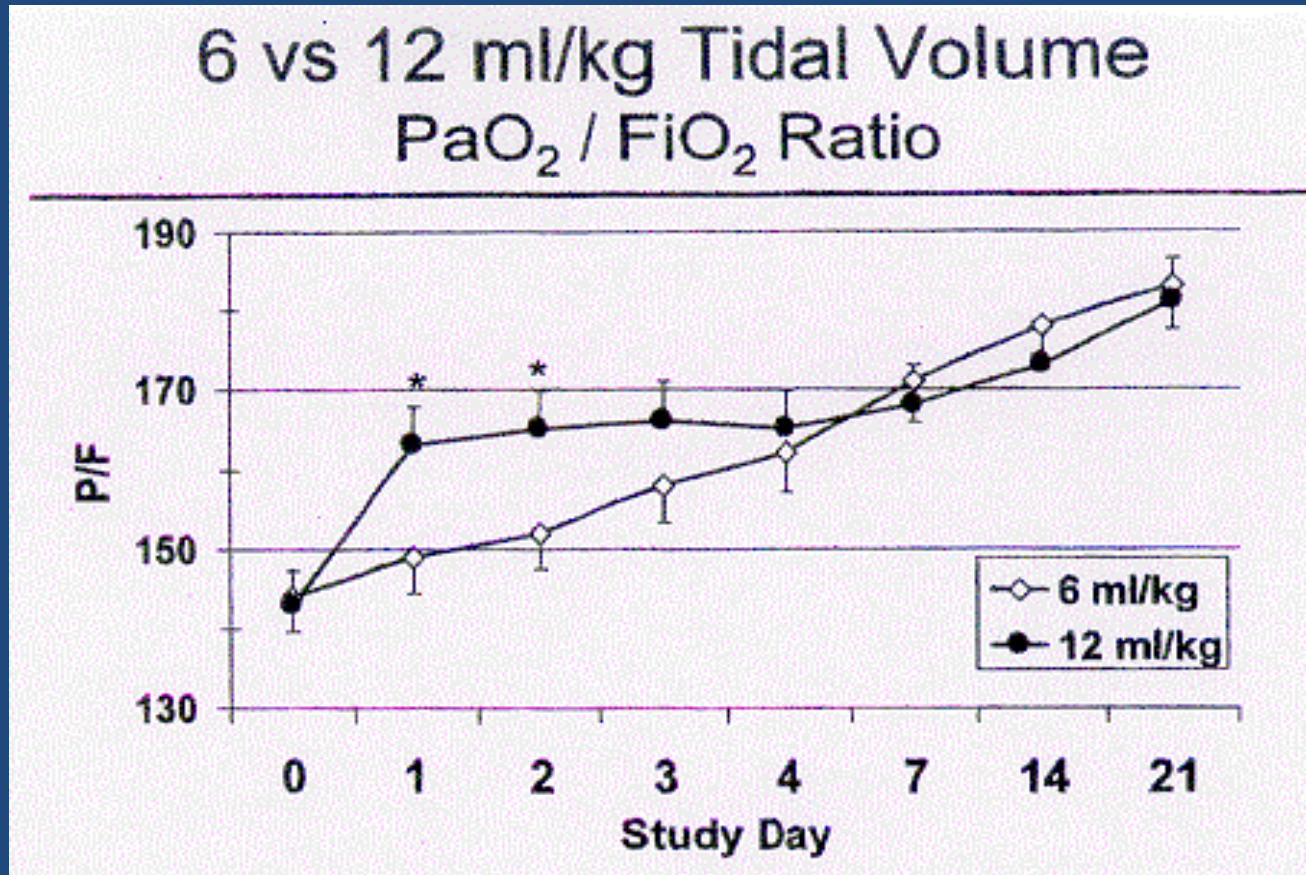


ARDSnet rules allowed pH values as low as 7.15

Question:

- What new MV strategy was shown to *worsen* gas exchange?
 - A. Pressure controlled inverse ratio ventilation
 - B. Airway pressure release ventilation
 - C. NIH ARDSnet low tidal volume strategy
 - D. High frequency oscillation
 - E. Adaptive support ventilation

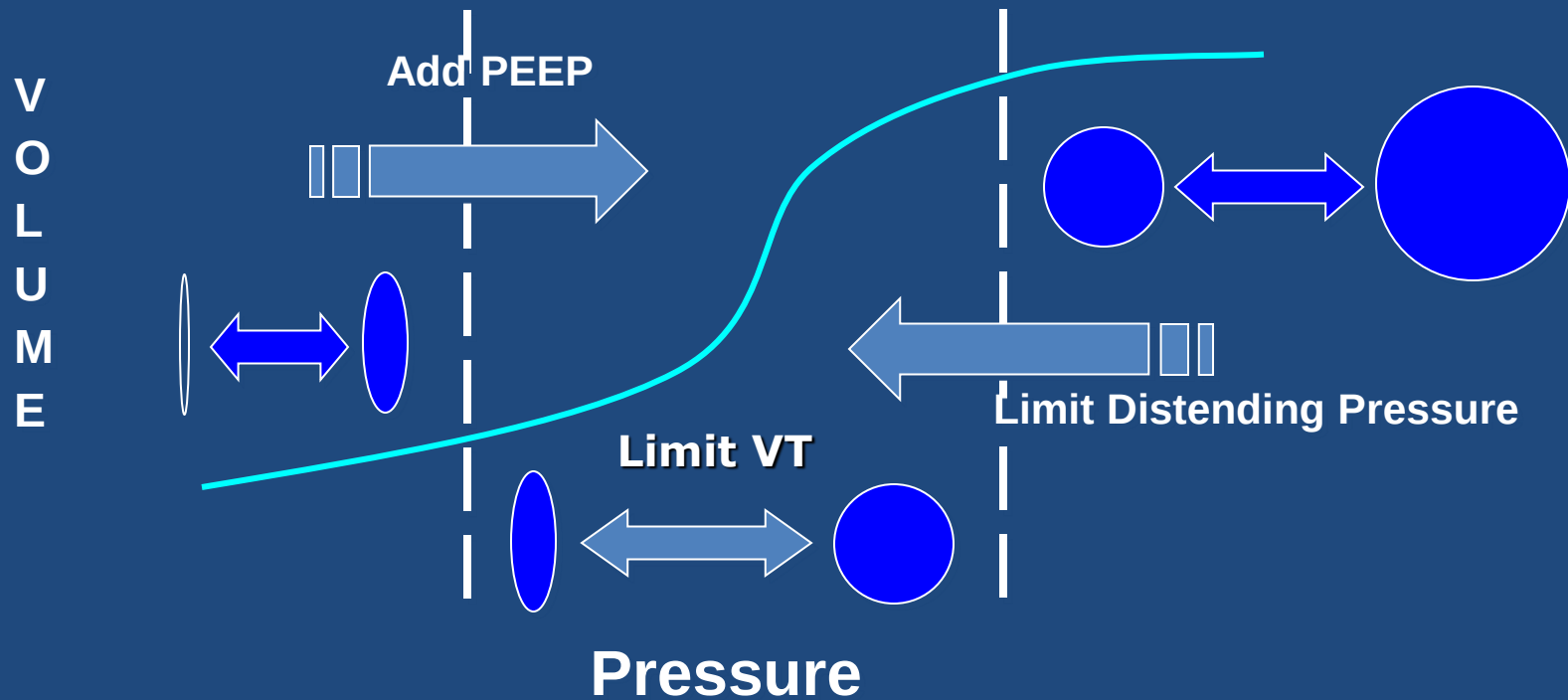
Balancing lung protection vs oxygenation

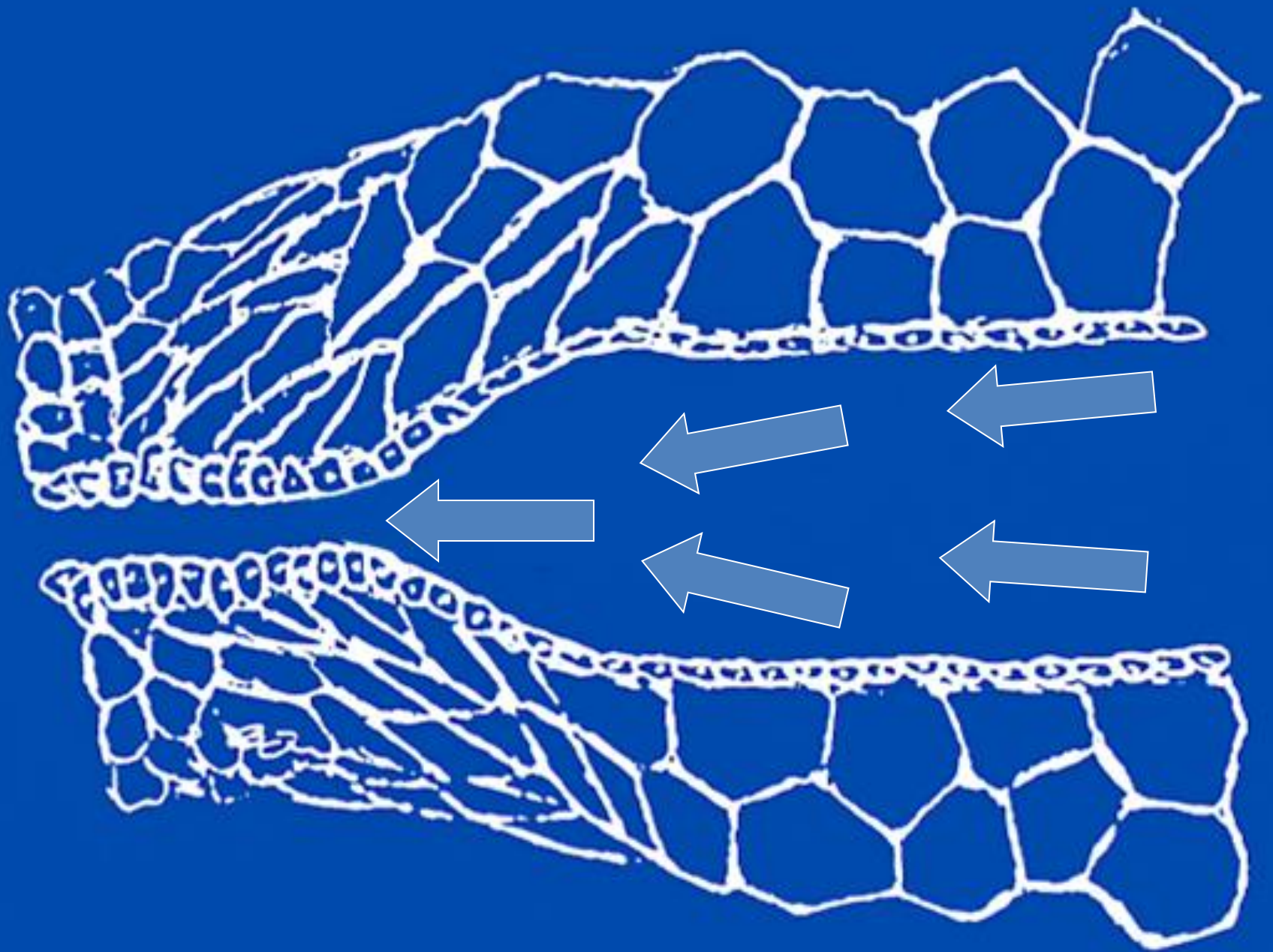


Crs also better in the HIGH Vt group

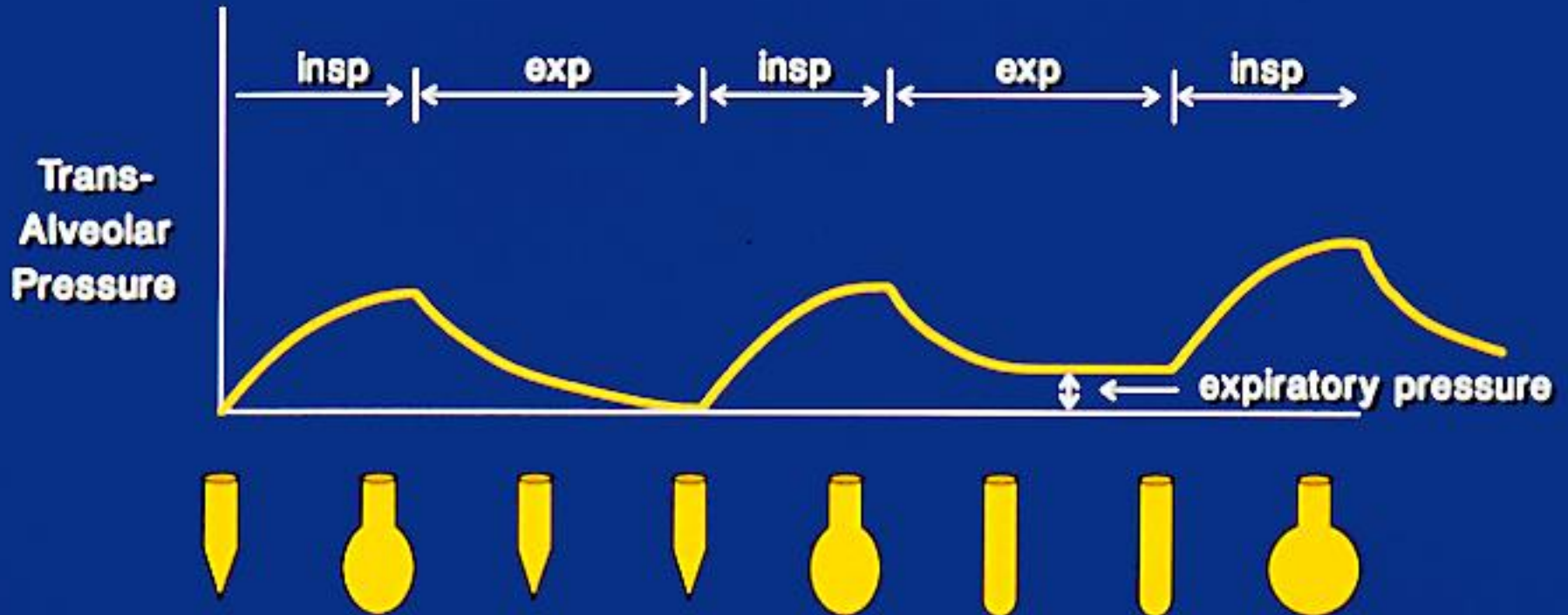
Preventing Overdistention and Collapse Injury

“Lung Protective” Ventilation





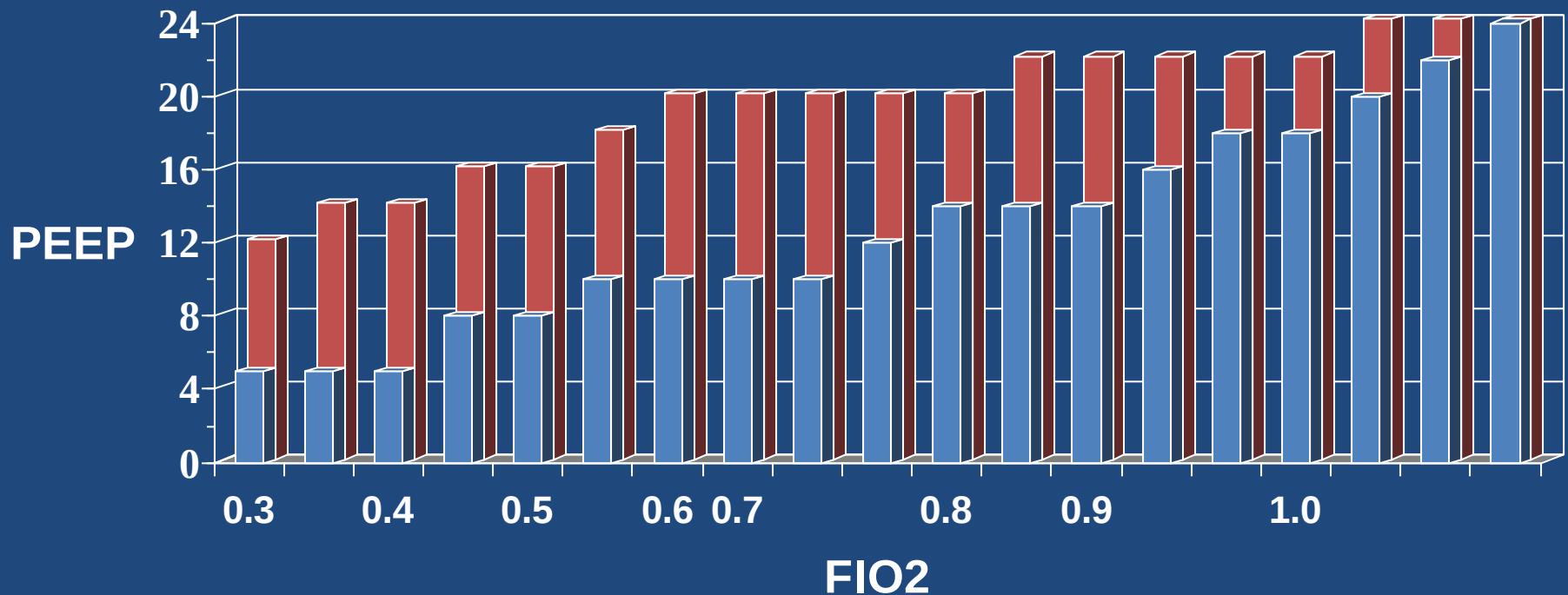
Recruit Alveoli (actually prevent de-recruitment)



Approaches to Setting PEEP/FiO₂

- Visual
 - CT, EIT
- Mechanical
 - PV curves, “Best” compliance, Pes, Stress Index
- Gas exchange
 - PEEP/FiO₂ Tables
 - “Juggling three balls” – PO₂, FiO₂, pressure
 - Goal is “adequate”, not “maximal” PaO₂, tradeoffs with FiO₂ and pressure depends on clinical bias

NIH ARDS Network PEEP-FiO2 Tables



Target: PO2 55-80
Plat < 30-35

Three RCTs: High vs Low PEEP Tables:

ARDS Net (n=585), Canadian (n=983) European (n=767)

NEJM 2004;351:327, *JAMA 2008;299:637, **JAMA 2008;299:644

	Low PEEP	High PEEP	
PEEP			
ARDSNet	8.9	14.7	
Canadian	10.1	15.6	
European	7.1	14.6	
Crs			
ARDSNet	.44	.55	
Canadian	.46	.46	
European	.44	.47	
PaO2/FiO2			
ARDSNet	168	222	
Canadian	149	187	
European	150	218	



Good

Three RCTs: High vs Low PEEP Tables:

ARDS Net (n=585), Canadian (n=983) European (n=767)

NEJM 2004;351:327, *JAMA 2008;299:637, **JAMA 2008;299:644

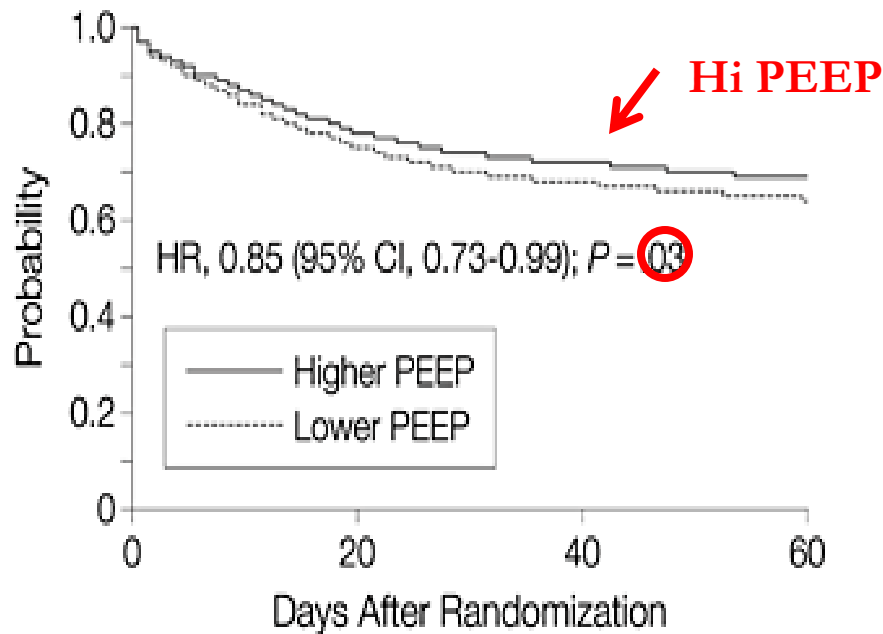
	Low PEEP	High PEEP	
PEEP			
ARDSNet	8.9	14.7	
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European	7.1	14.6	
Crs			
ARDSNet	.44	.55	
Canadian	.46	.46	
European	.44	.47	
PaO ₂ /FiO ₂			
ARDSNet	168	222	
Canadian	149	187	
European	150	218	
Pplat			
ARDSNet	24.0	27.0	
Canadian	24.9	30.2	
European	21.1	27.5	

Good

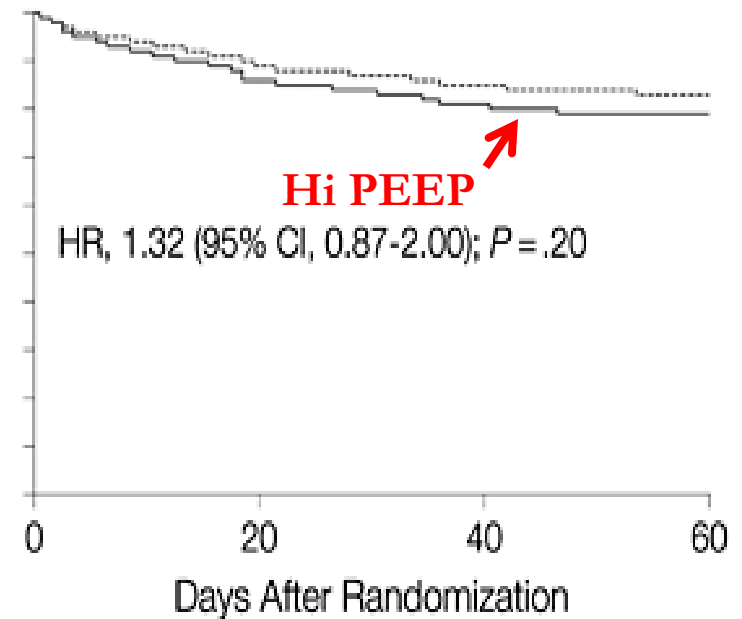
Bad

In-hospital time to death

Patients with ARDS

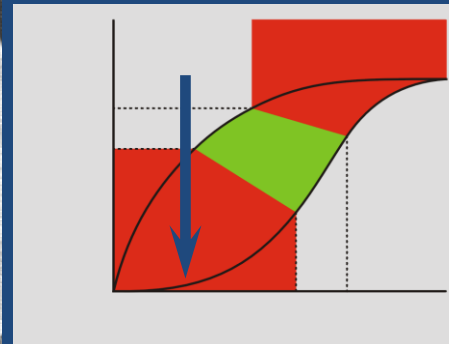
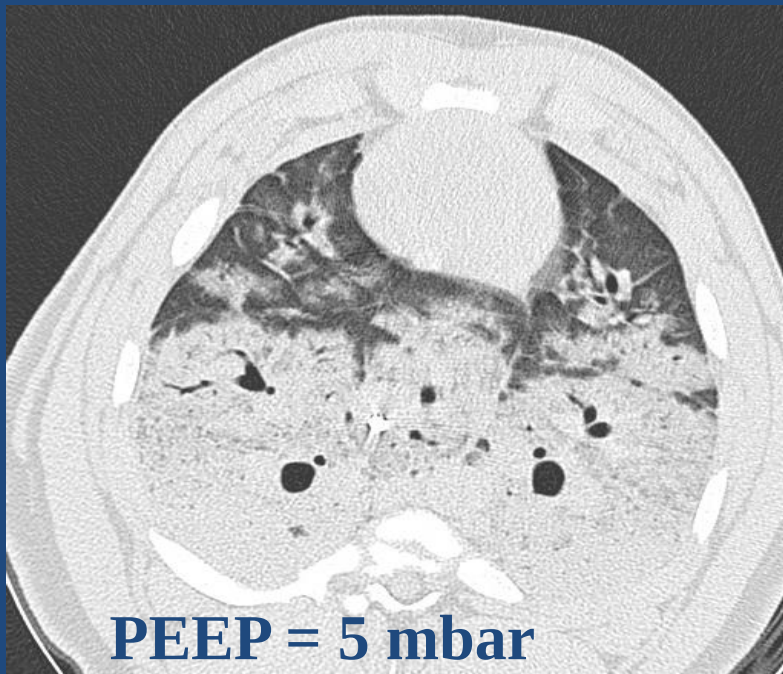
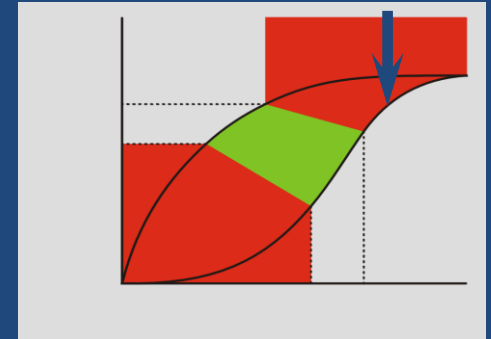
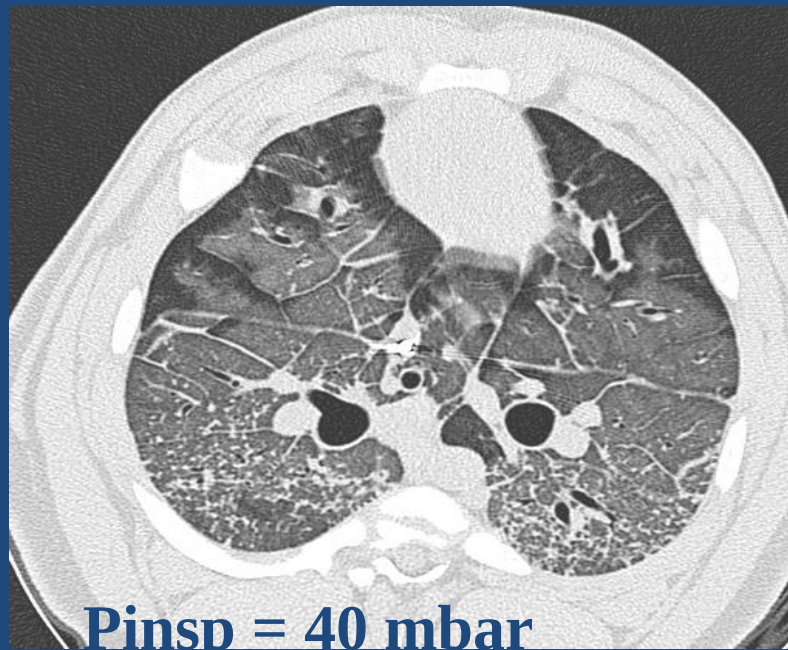


Patients without ARDS



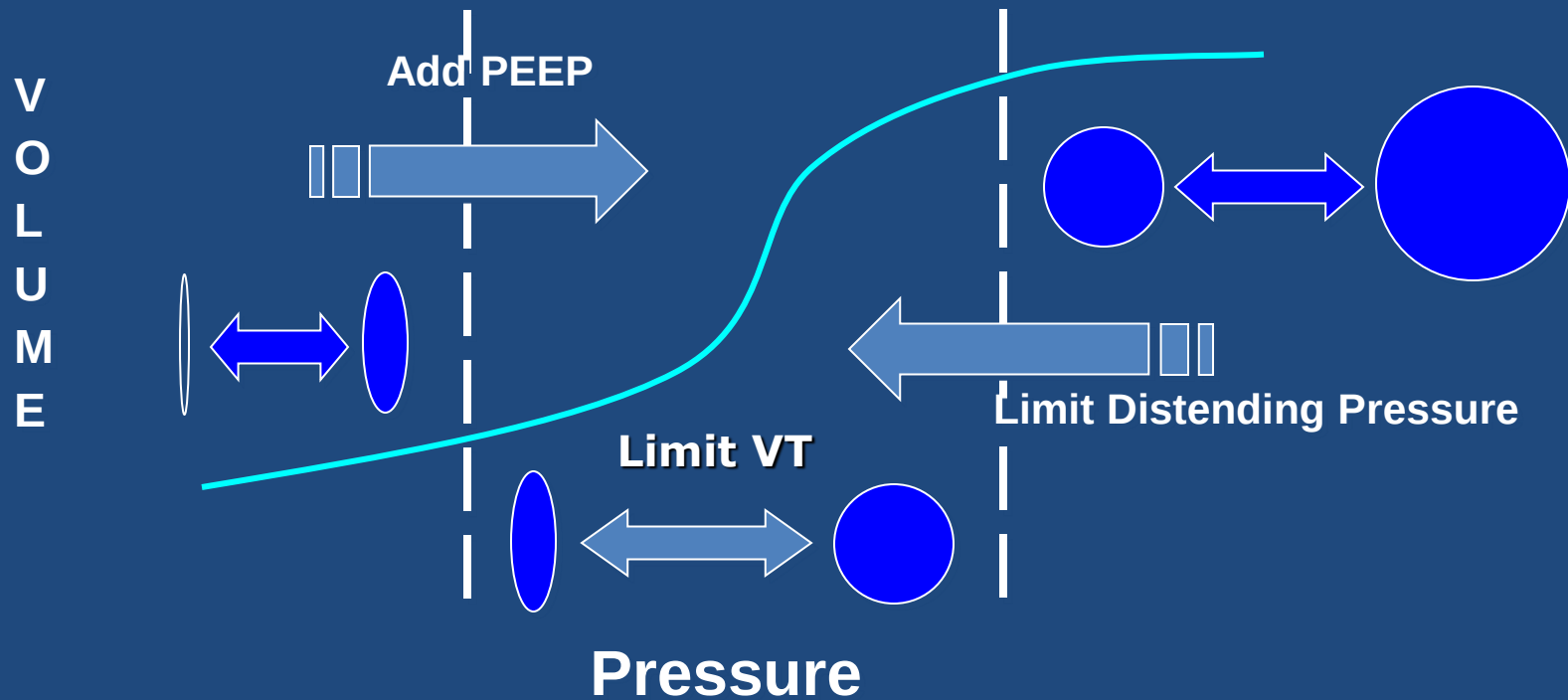
No. at risk

Higher PEEP	949	760	693	666	183	158	148	144
Lower PEEP	939	723	649	619	219	196	186	183



Preventing Overdistention and Collapse Injury

“Lung Protective” Ventilation



Mechanical Ventilation:

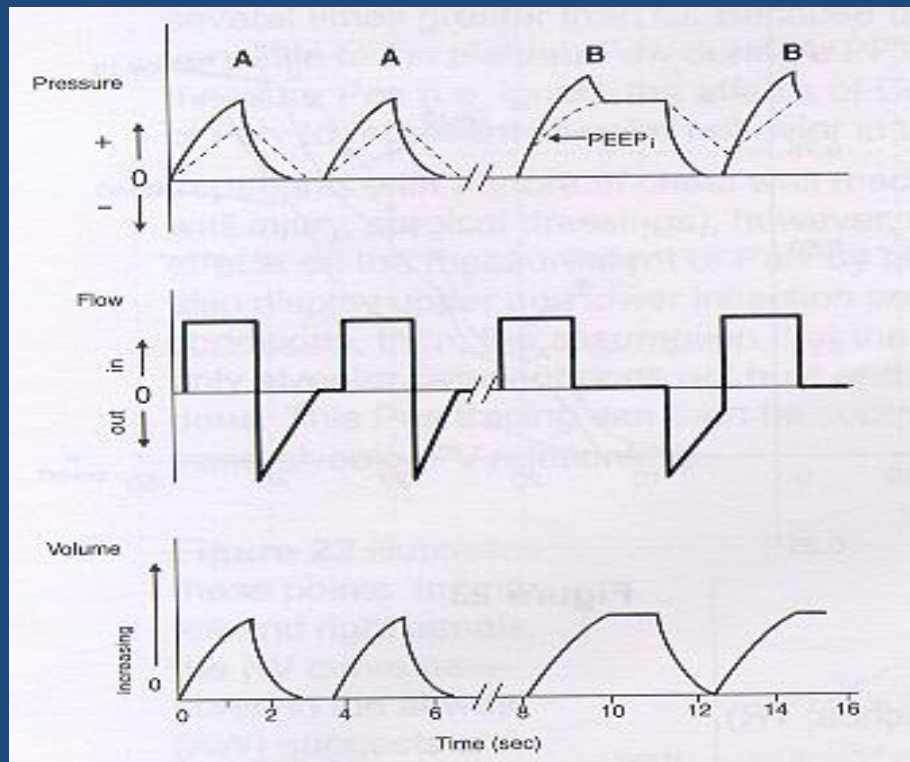
Clinical Challenges 2012

- Lung protection
- Intrinsic PEEP
- Patient ventilator synchrony
- Maintaining cardiac function
- Prompt discontinuation

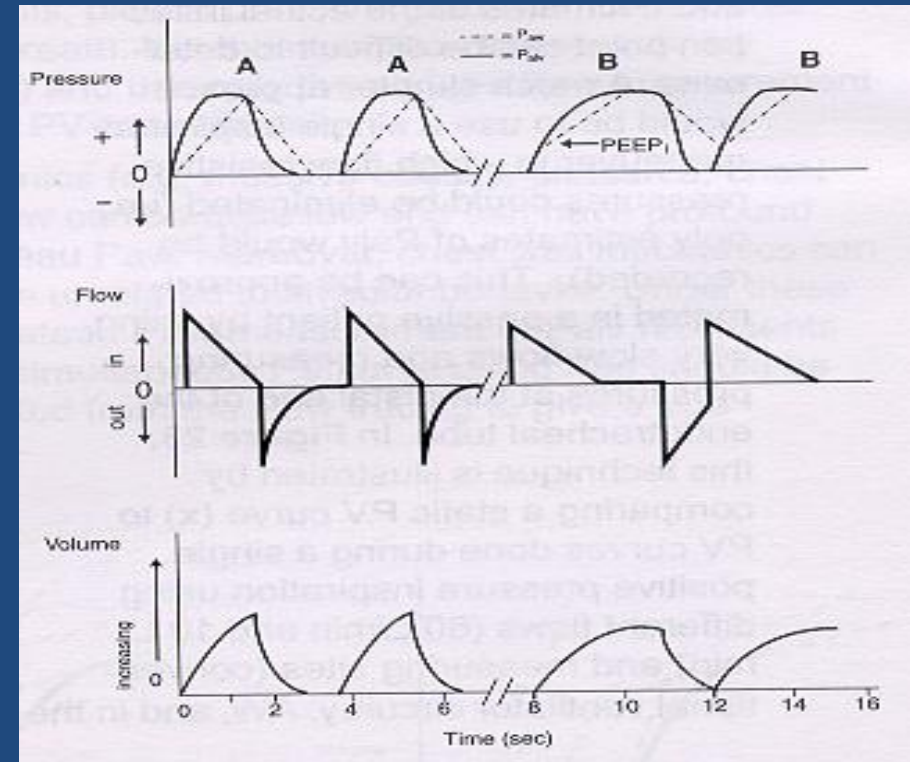
Air trapping-PEEPi

- Determinants
 - Minute ventilation
 - I:E ratio
 - Exp time constant ($R \times C$)
- Effects:
 - Increases end expiratory volume - with constant V_T , will raise P_{peak} , P_{plat} - with constant P_i , will lower V_T
 - Inspiratory threshold load

PEEPi affects VACV and PACV differently



VACV

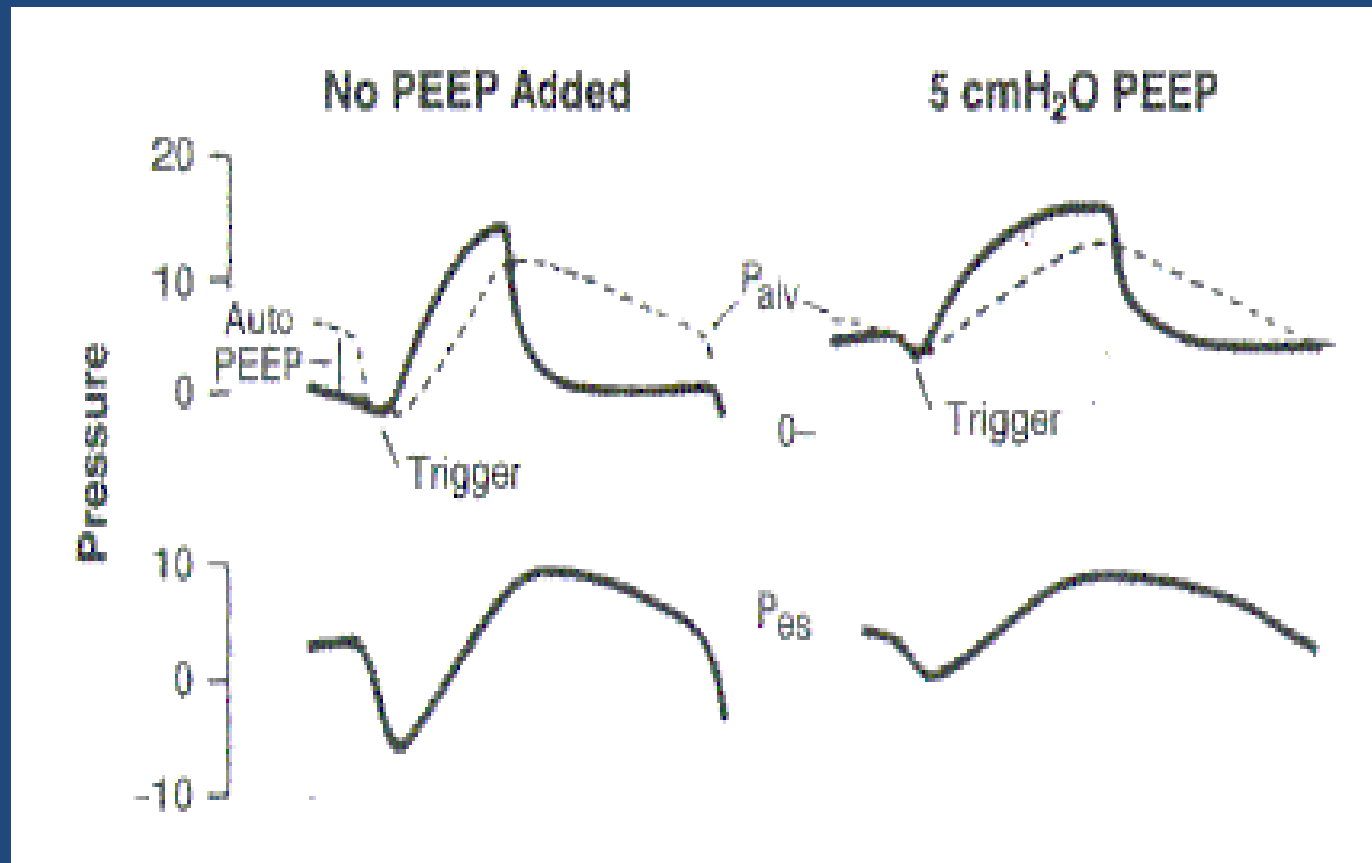


PACV

Air trapping-PEEPi

- PEEPi determined by 3 factors:
 - MV (f, Vt equal)
 - I:E
 - Mechanics: hi R, hi C
- Therefore, to fix it:
 - Decrease MV (either f or Vt)
 - Shorten I:E
 - Improve mechanics

PEEPi functions as an inspiratory threshold load

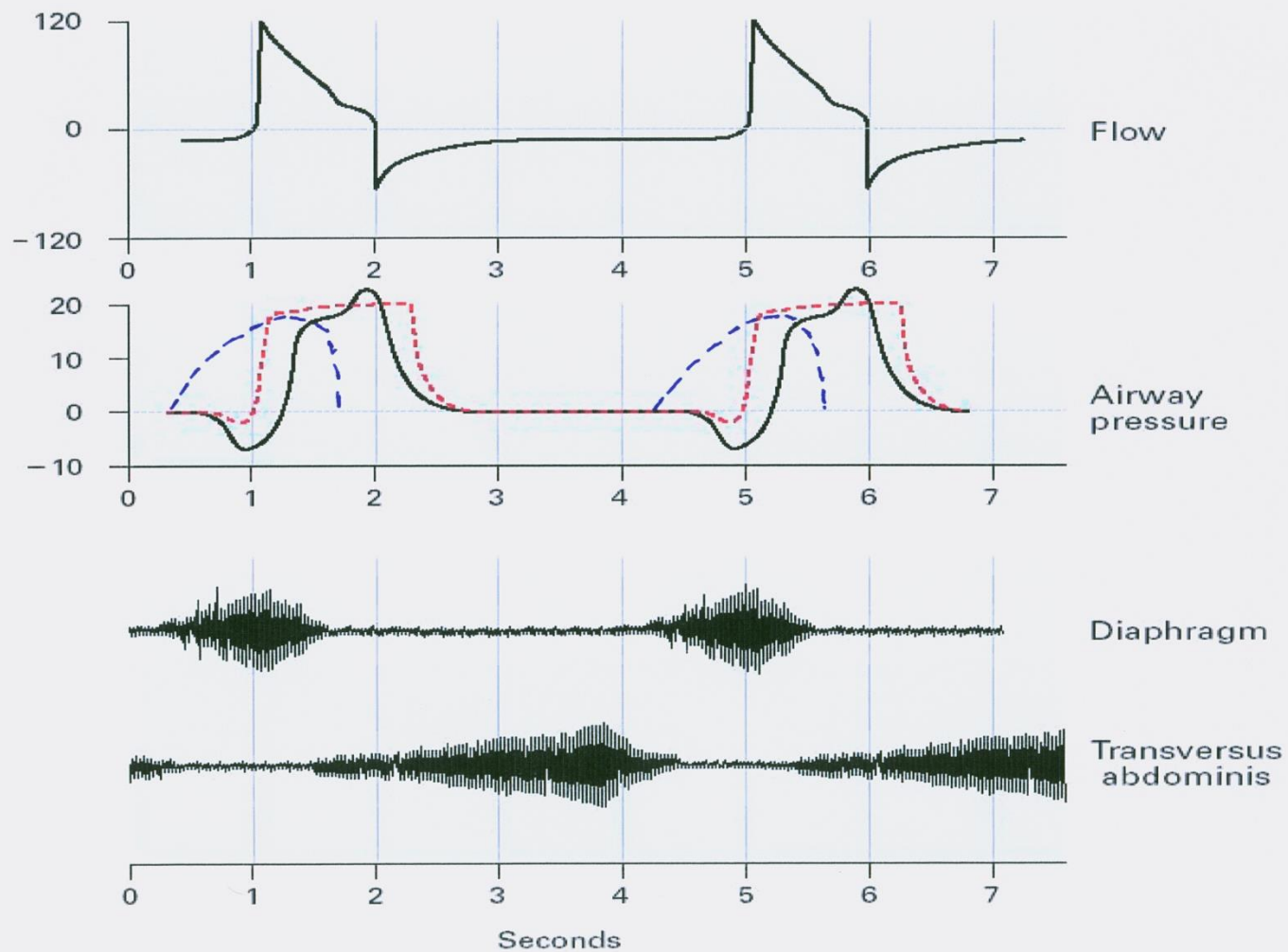


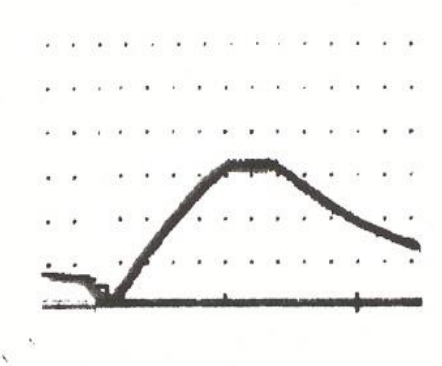
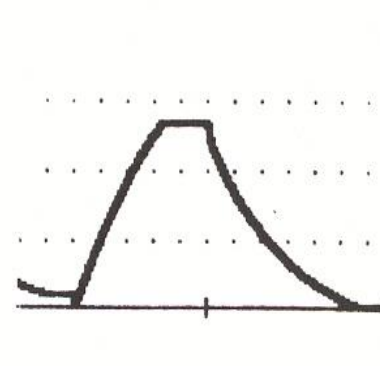
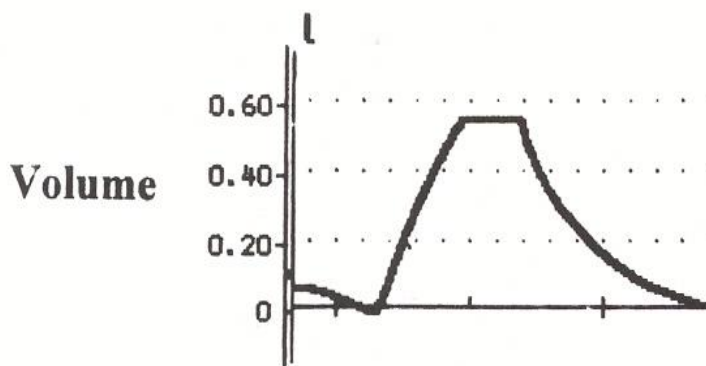
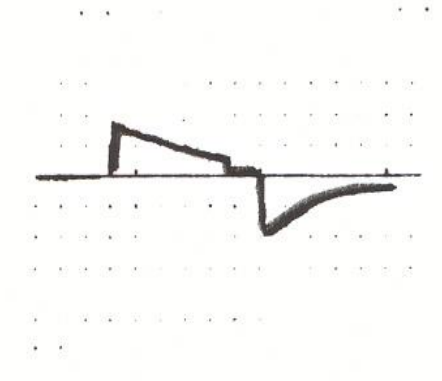
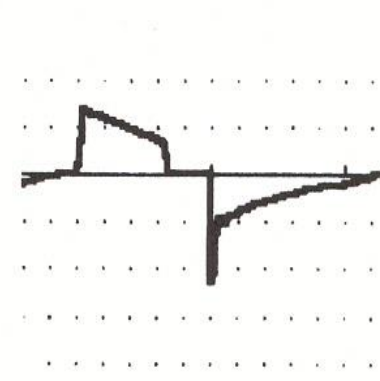
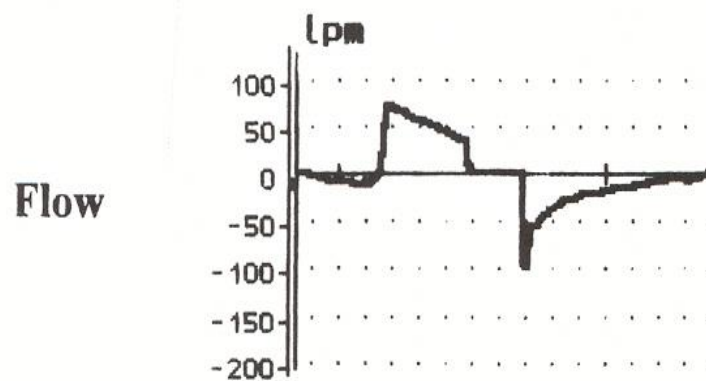
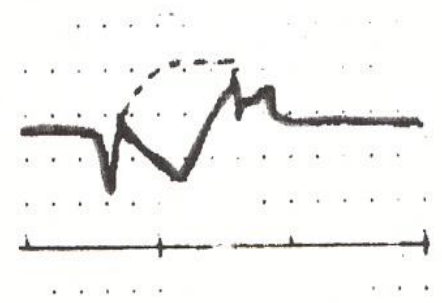
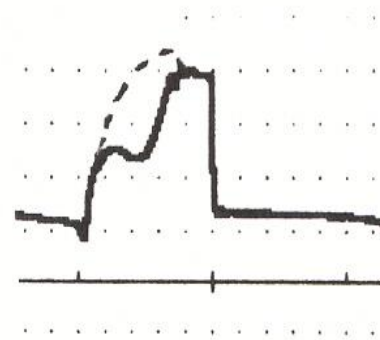
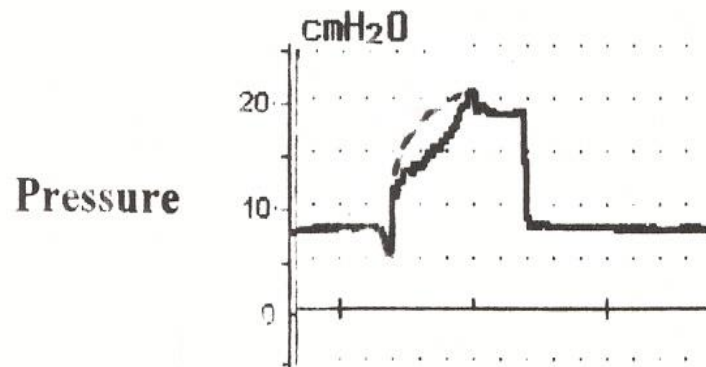
Mechanical Ventilation:

Clinical Challenges 2012

- Lung protection
- Intrinsic PEEP
- Patient ventilator synchrony
- Maintaining cardiac function
- Prompt discontinuation

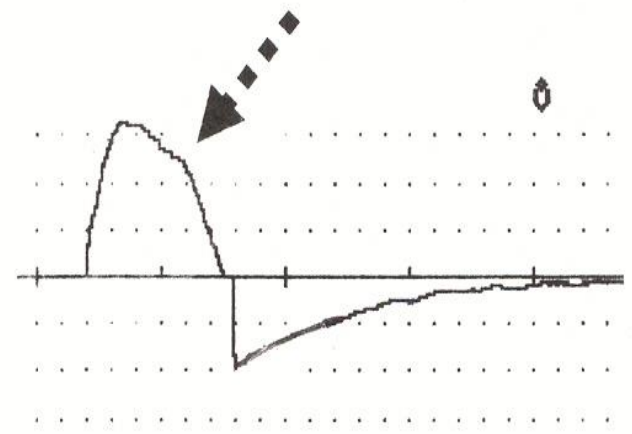
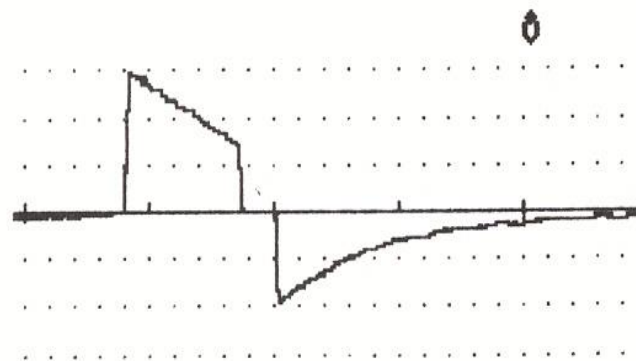
Trigger Flow Cycle



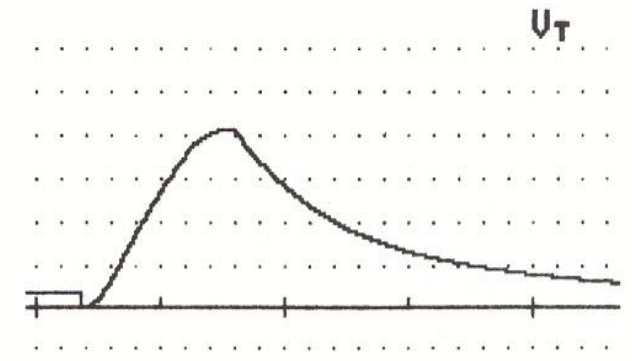
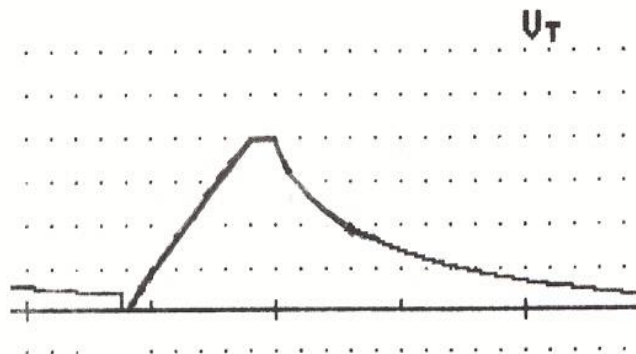


Time

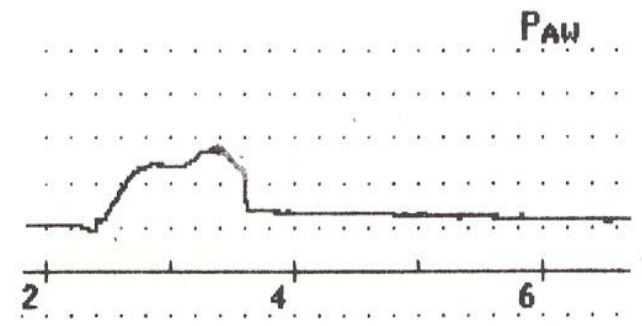
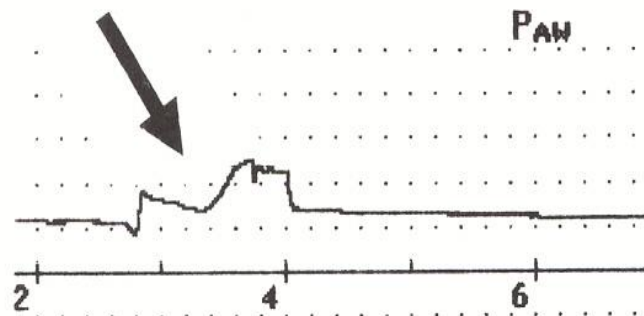
Flow



Volume



Pressure



Newer approaches to improving synchrony

- Proportional assist ventilation
 - Pressure and flow driven by sensed pt flow
- Neurally adjusted ventilator assistance
 - Pressure and flow driven by diaphragm EMG

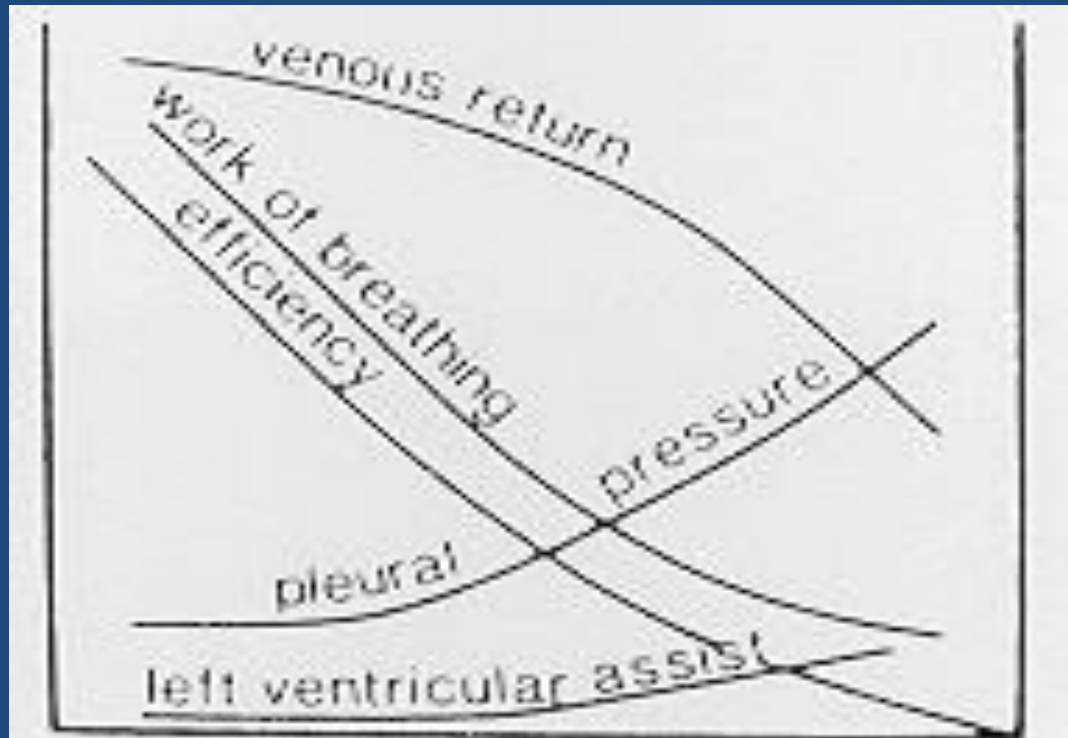
Both have theoretical appeal and have been shown to support patient effort – However, no meaningful outcome data

Mechanical Ventilation:

Clinical Challenges 2012

- Lung protection
- Intrinsic PEEP
- Patient ventilator synchrony
- Maintaining cardiac function
- Prompt discontinuation

Effects of Increasing Positive Airway Pressure



Low (Unassisted) → High (Controlled)

Level of Applied Pressure

Mechanical Ventilation and Cardiac Function

- Positive intrathoracic pressure can be harmful:
 - If intravascular volume low, reduced cardiac filling leads to reduced cardiac output
- Positive intrathoracic pressure can be helpful:
 - If intravascular volume high, reduced cardiac filling leads to less edema formation
 - Reduces LV afterload

Mechanical Ventilation:

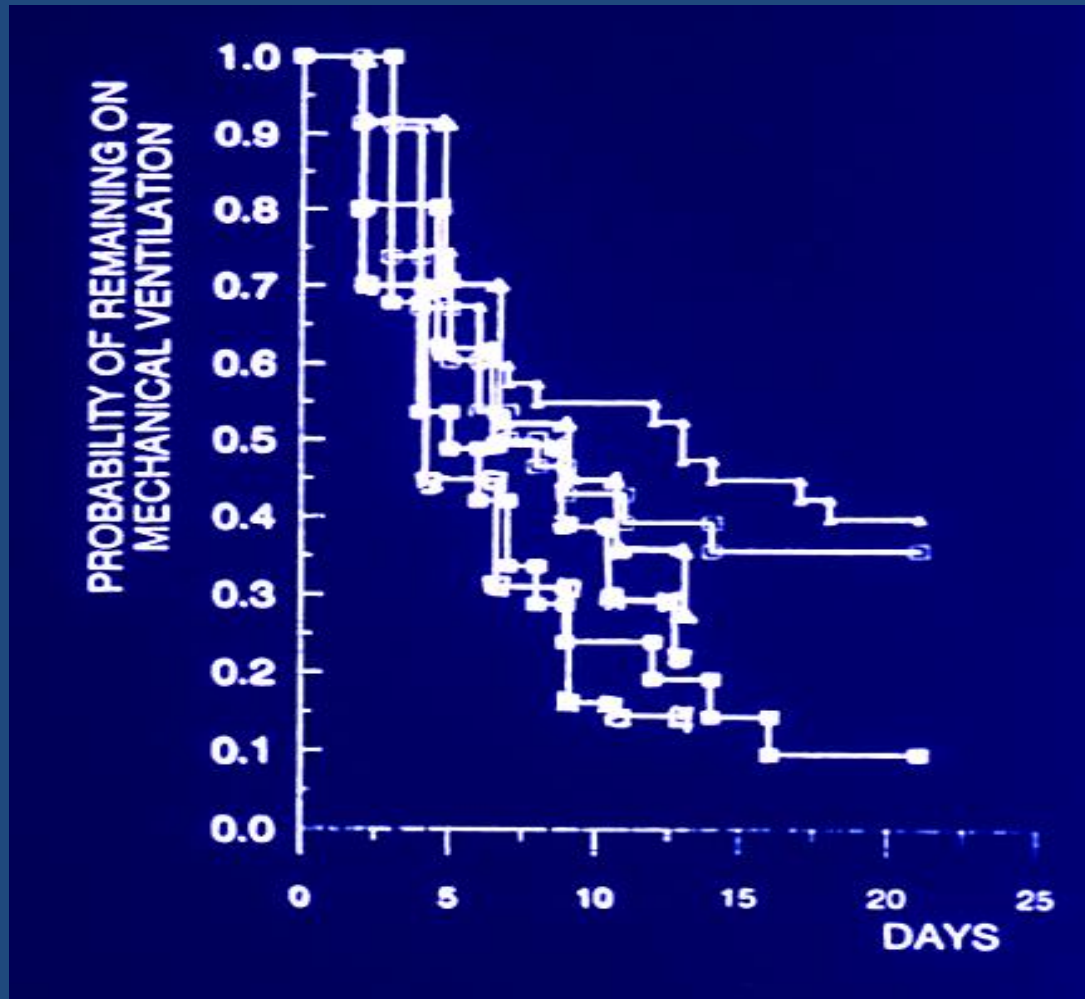
Clinical Challenges 2012

- Lung protection
- Intrinsic PEEP
- Patient ventilator synchrony
- Maintaining cardiac function
- Prompt discontinuation

Question:

- A patient is recovering from respiratory failure and is comfortable on 15 cm H₂O pressure support ventilation. What ventilator strategy has been shown to be most effective in the discontinuation process?
 - A. Gradual reductions in pressure support to <5cm H₂O over 48-72 hours
 - B. Switch to SIMV and gradually reduce SIMV rate to <4 over 48-72 hours
 - C. Add SIMV and gradually reduce in SIMV rate to <4 + pressure support to <5cm H₂O
 - D. Gradual increases in t-piece breathing periods starting at 5-10 minutes and increasing 5-10 minutes daily until 2 hours tolerated
 - E. Daily 30-120 minute spontaneous breathing trials without further ventilator manipulations

No strategy has been shown to be faster than daily SBTs



ACCP/SCCM/AARC EBM Guidelines

- Criteria for considering vent discontinuation:
 - stability/reversal of ARF
 - $P/F > 150-200$, $PEEP < 5-8$, $FiO_2 < 0.4-0.5$, $pH > 7.25$
 - hemodynamic stability ($dop/dob < 5$)
 - capable of reliable insp efforts

ACCP/SCCM/AARC EBM Guidelines

- SBT is most effective way of assessing d/c potential:
 - 30-120 min
 - 5 cm H₂O PS reasonable
 - 1st 1-5 minutes needs close monitoring
 - vent pattern (eg resp rate), gas exchange, hemodynamic stability, comfort
- Other “traditional” indices (eg MV, VC, NIF, P0.1), while predictive in large populations, are poor individual predictors

ET tube removal requires ability to protect airway

- Cough is essential
 - Cough velocity (>1 l/sec)
 - White card test
 - Suctioning frequency
- Less important:
 - Gag reflex present
 - Cuff leak
 - Alertness

ACCP/SCCM/AARC EBM Guidelines

- For patients who fail the SBT:
 - Search for reversible causes
 - Repeat SBTs q 24 hrs in those maintaining clinical stability
 - In between, provide *stable* and comfortable assisted ventilation
 - Little data demonstrating gradual support reduction reduces VLOS – likely wastes resources and risks fatigue

Protocols run by non-MDs effective!

Mechanical Ventilation:

Clinical Challenges

- Lung protection
- Intrinsic PEEP
- Patient ventilator synchrony
- Maintaining cardiac function
- Prompt discontinuation

Mechanical Ventilation III: Managing the Ventilator and Weaning



E. Wesley Ely, MD, MPH, FCCP

Professor of Medicine

Division of Pulmonary/Critical Care & Health Services Research

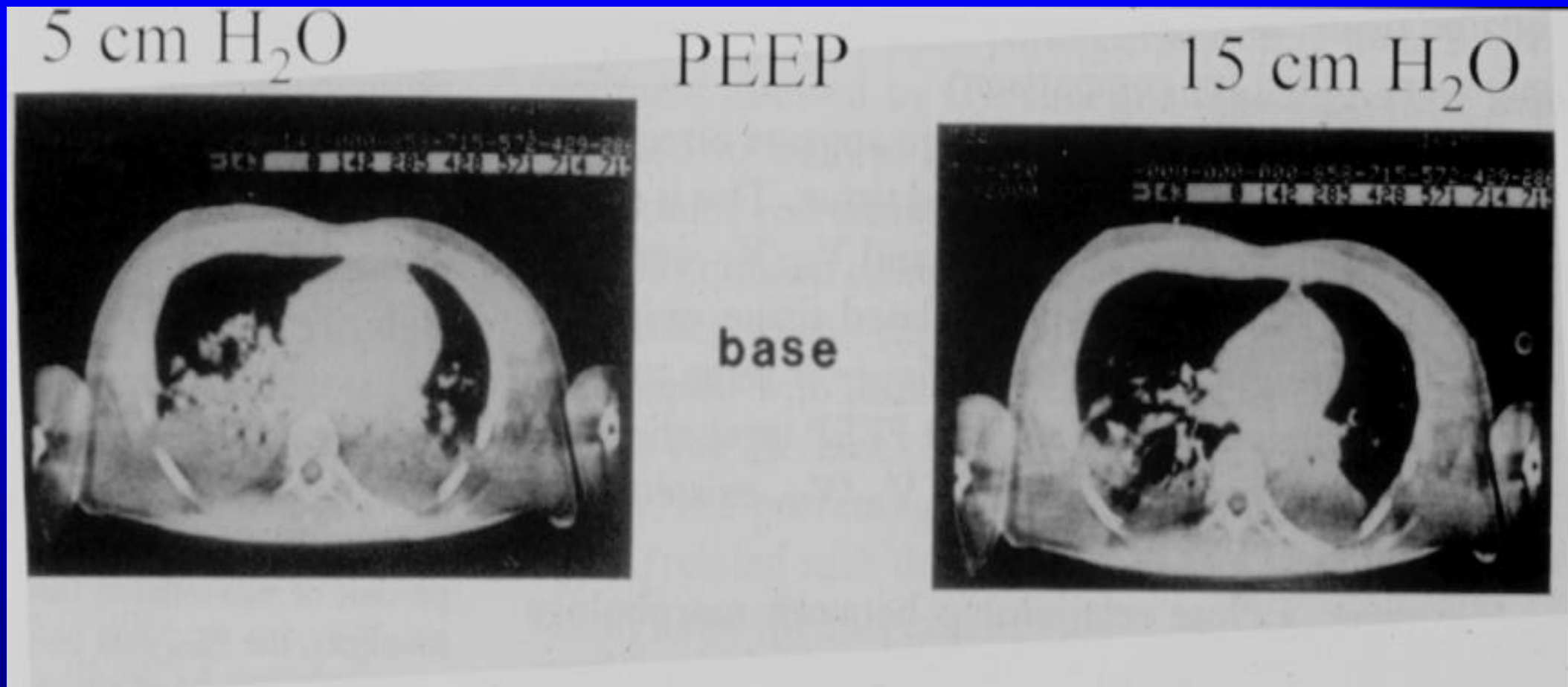
Associate Director of Geriatric Research (GRECC)

Vanderbilt University, Nashville, TN

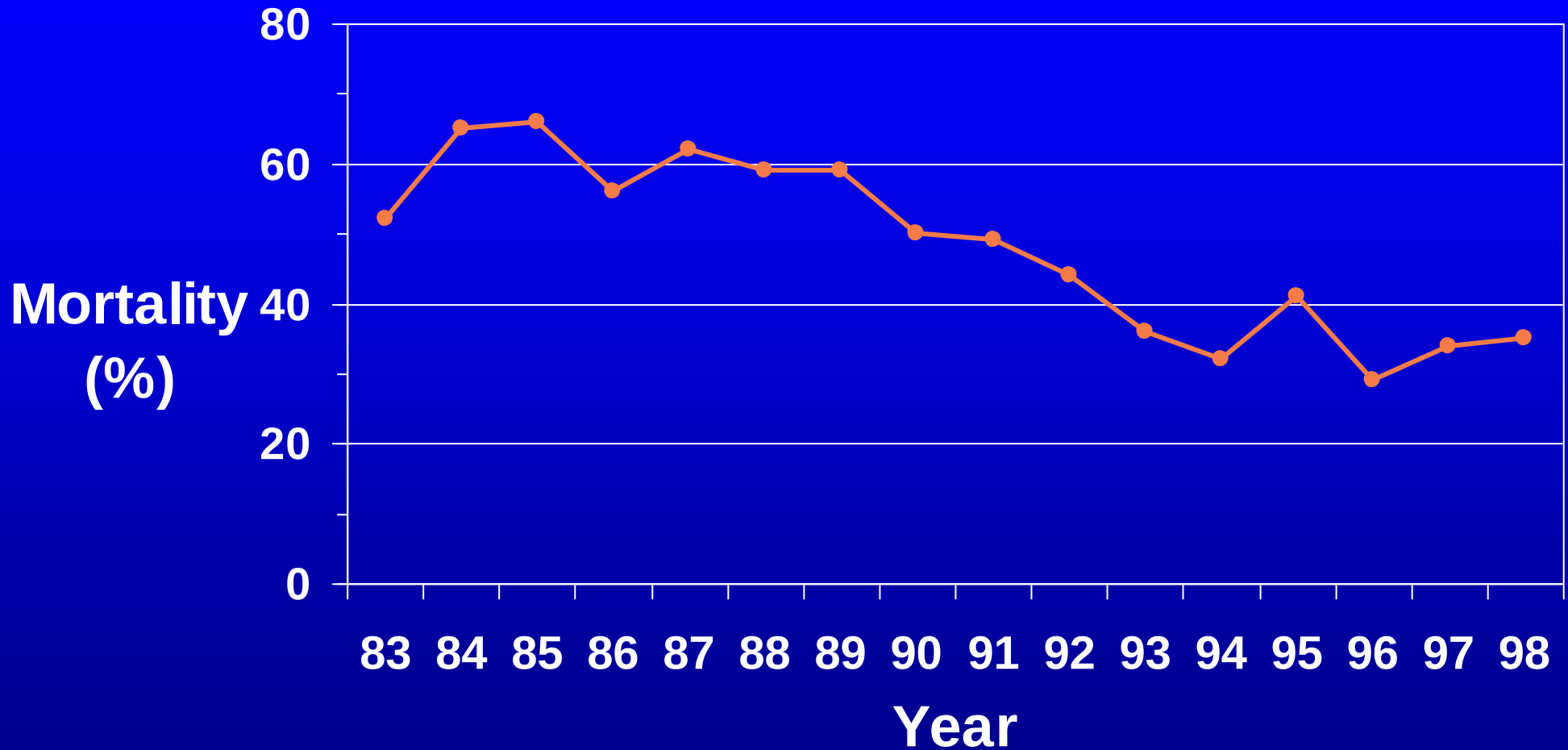
Acute Lung Injury / ARDS



Acute Lung Injury is Heterogeneous



Mortality in ARDS



Milberg JAMA 1995; 273:306

Phua et al, AJRCCM 2009;179:220-27

Acute Lung Injury / ARDS

Berlin Definition

- Clinical Prediction Rule derived/validated on 4,188 pts
- Mild/Mod/Severe ARDS had mortalities of 27%, 32%, and 45% ($p < 0.001$)
- Mild/Mod/Severe ARDS had LOS on ventilator of 5 vs 7 vs 9 days ($p < 0.001$)
- Compared to previous AECC definition, AUC was 0.58 vs. 0.54 ($p < 0.001$)

JAMA 2012;307:2526-2533

Angus D, JAMA 2012;307:2542-44

Ferguson N, ICM 2012;38:1573-82

Acute Lung Injury / ARDS

Berlin Definition

- Changes include
 1. Acute defined as 1 week
 2. Term ALI abandoned (was confusing and variably defined)
 3. P/F ratio now requires specific minimum PEEP 5
 4. 3 categories of ARDS based on P/F
 <300 (mild), <200 (moderate), and ≤ 100 (severe)
 5. CXR criteria improved
 6. PCWP criteria removed with more practical exclusion of CV dz

JAMA 2012;307:2526-2533

Angus D, JAMA 2012;307:2542-44

Ferguson N, ICM 2012;38:1573-82

P/F Predictor Calculator

URL - <http://data.vanderbilt.edu/predictor/>

Estimated PaO₂/FiO₂

SpO₂ , FiO₂ , Age years , Ventilator , PEEP
cms H₂O , Temp

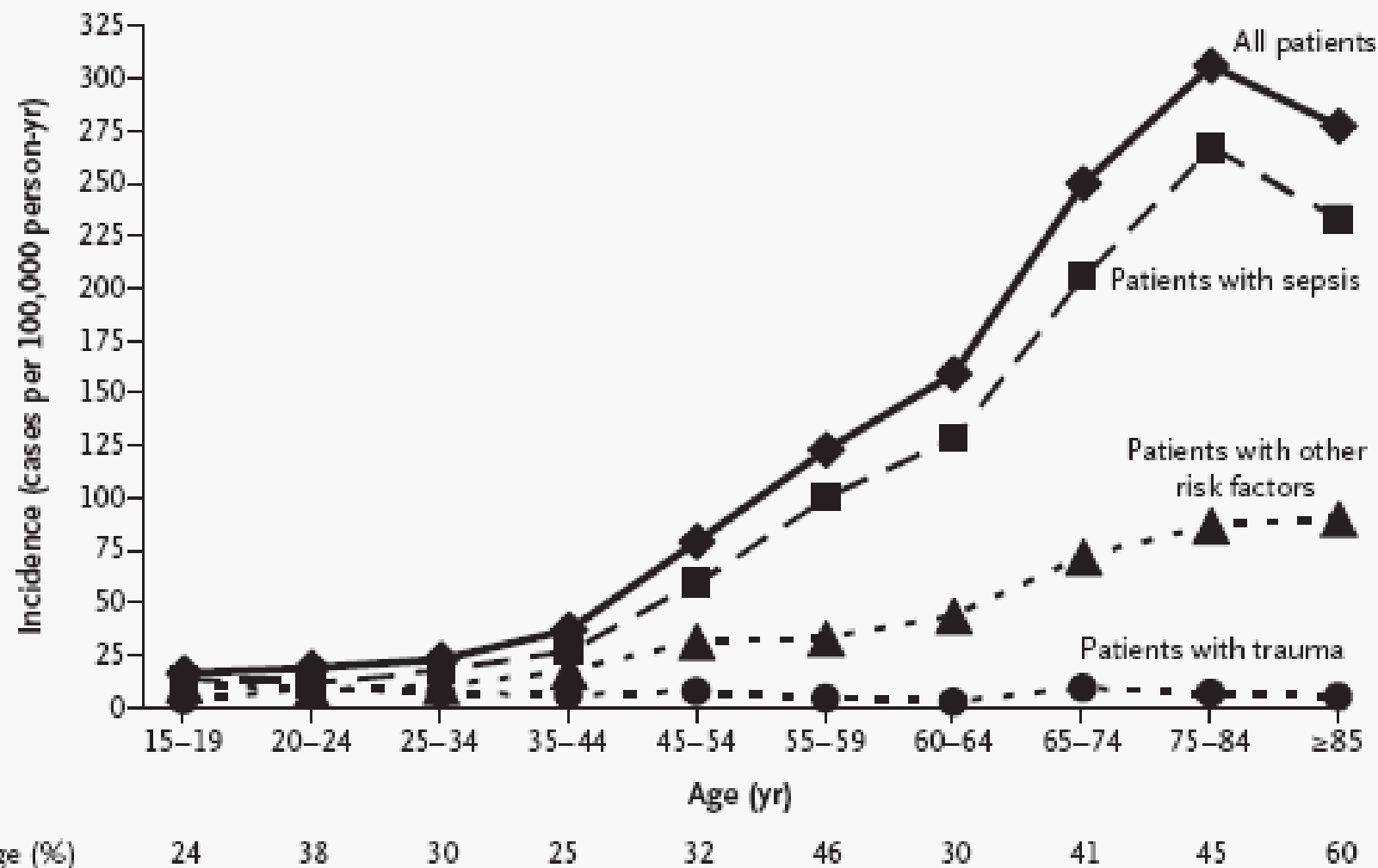
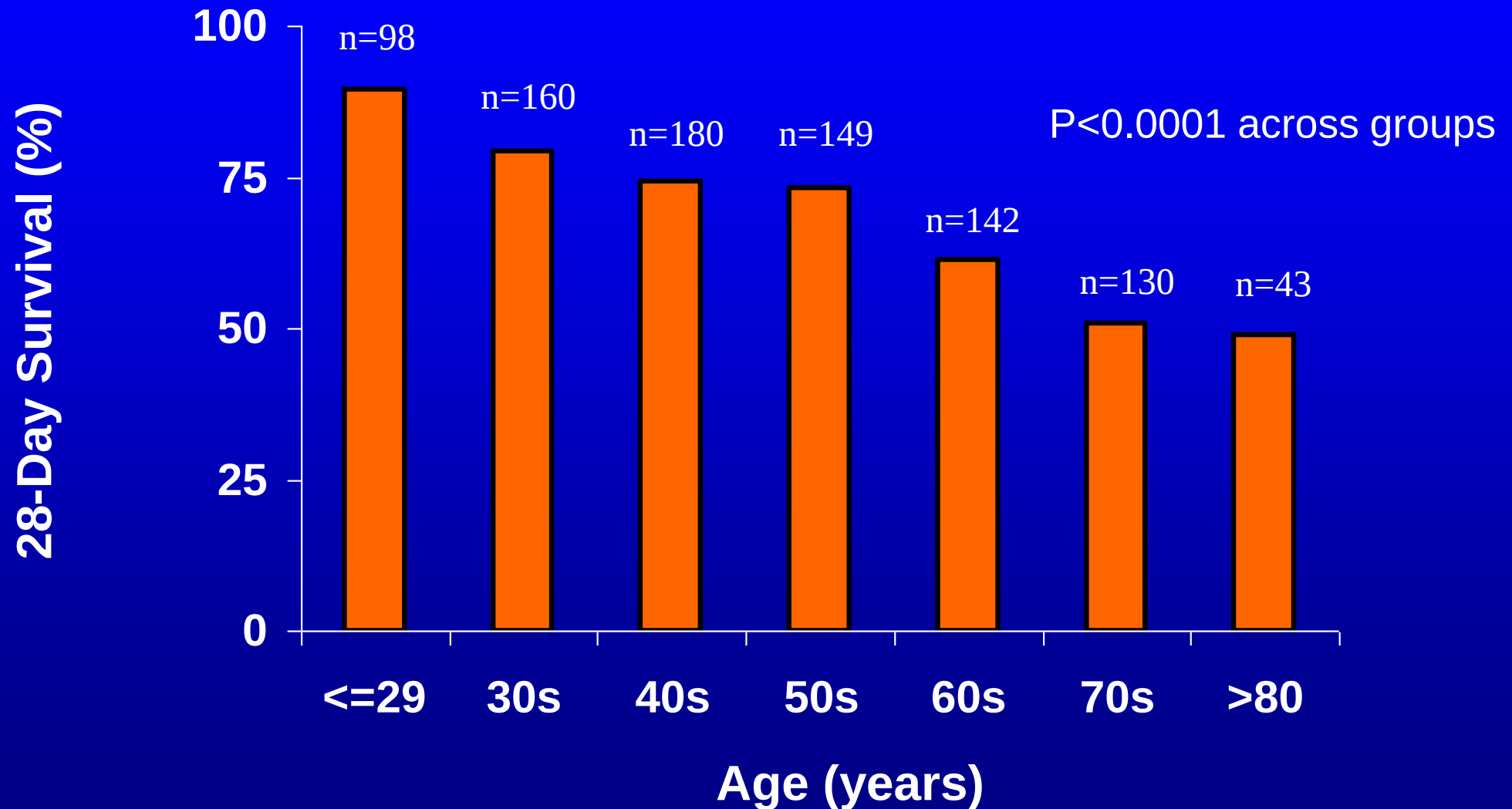


Figure 2. Age- and Risk-Specific Incidence of and Age-Specific Mortality from Acute Lung Injury.

Risk-factor categories are not mutually exclusive; $P < 0.001$ for trend for the comparison of age-specific mortality rates.

ARDSNet Survival from ALI/ARDS by Age



Quality of Survival Post-ARDS

- Many surviving ARDS patients are unable to return home at hospital discharge
- Survivors of ARDS have generalized weakness, pulmonary dysfunction, cognitive disability, affective disorders, and reduced quality of life after an episode of critical illness
- Attention to the post-discharge phase of care is essential if we clinicians are to achieve the best possible outcomes.

- Nonpulmonary comorbidities may be main determinants of outcome in ARDS survivors
- Is the lung bone connected to the brain bone?

Tour of ARDS-net Studies and Guidelines



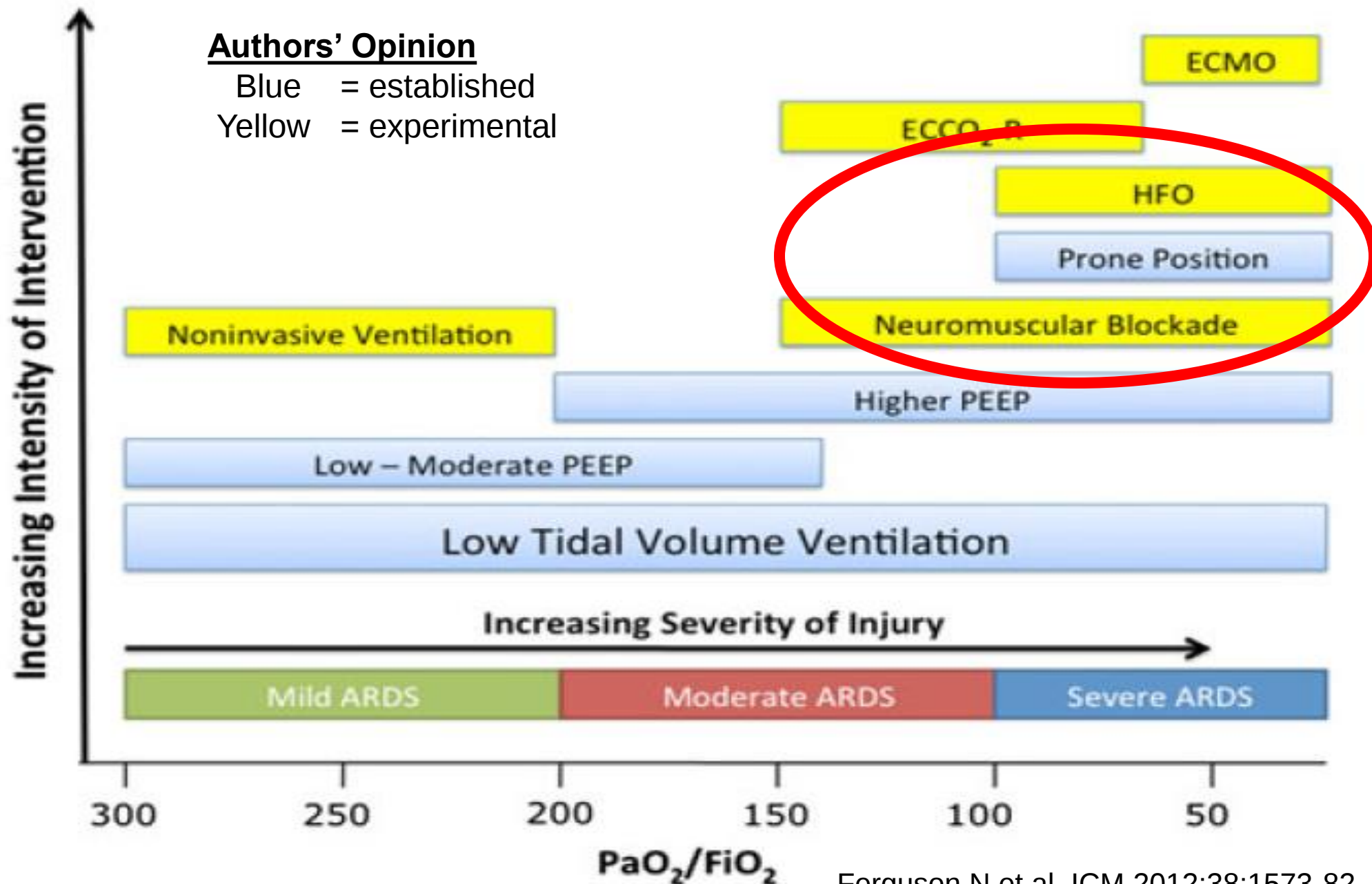
What do we know is good...

Sepsis-induced ARDS

- Volume A/C or PCV with
 - Maintain PO₂ between 55-80 mmHg (sats 88-95%)
 - PEEP, higher rather than lower (grade 1)
 - Vt between 4-8 ml/kg IBW (grade 1)
 - Plt Pressure $\leq$ 30 cm H₂O (grade 1)
 - Permissive hypercapnea (grade 1)
 - Head of Bed elevated (grade 1)
 - Don't use a PAC (grade 1)
 - Conservative fluids once out of shock (grade 1)

Management of Sepsis-induced ARDS ...

- Sedation and paralysis....
 - Weaning protocols with SBTs (grade 1)
 - Sedation protocols and minimization of sedation (grade 1)
 - Best way to minimize is with SATs (Kress NEJM, Girard, Lancet 2008)
- Controversial / Ancillary Management Options...
 - Prone positioning (grade 2)
 - Recruitment maneuvers (grade 2)
 - HFO (high frequency oscillation, OSCAR/OSCILLATE)
 - ECMO (Peek G for CESAR trial) Lancet 2009;374:1351-63
 - Routine neuromuscular blockade, NMB (grade 2)



Neuromuscular Blockade (NMB)

Effect of neuromuscular blocking agents on gas exchange in patients presenting with acute respiratory distress syndrome*

Marc Gainnier, MD; Antoine Roch, MD; Jean-Marie Forel, MD; Xavier Thirion, MD, PhD; Jean-Michel Arnal, MD; Stéphane Donati, MD; Laurent Papazian, MD, PhD

Gainnier CCM 2004

Neuromuscular blocking agents decrease inflammatory response in patients presenting with acute respiratory distress syndrome*

Jean-Marie Forel, MD; Antoine Roch, MD, PhD; Valérie Marin, MD, PhD; Pierre Michelet, MD; Didier Demory, MD; Jean-Louis Blache, MD; Gilles Perrin, MD; Marc Gainnier, MD, PhD; Pierre Bongrand, MD, PhD; Laurent Papazian, MD, PhD

Forel CCM 2006

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Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaél Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D.,
for the ACURASYS Study Investigators*

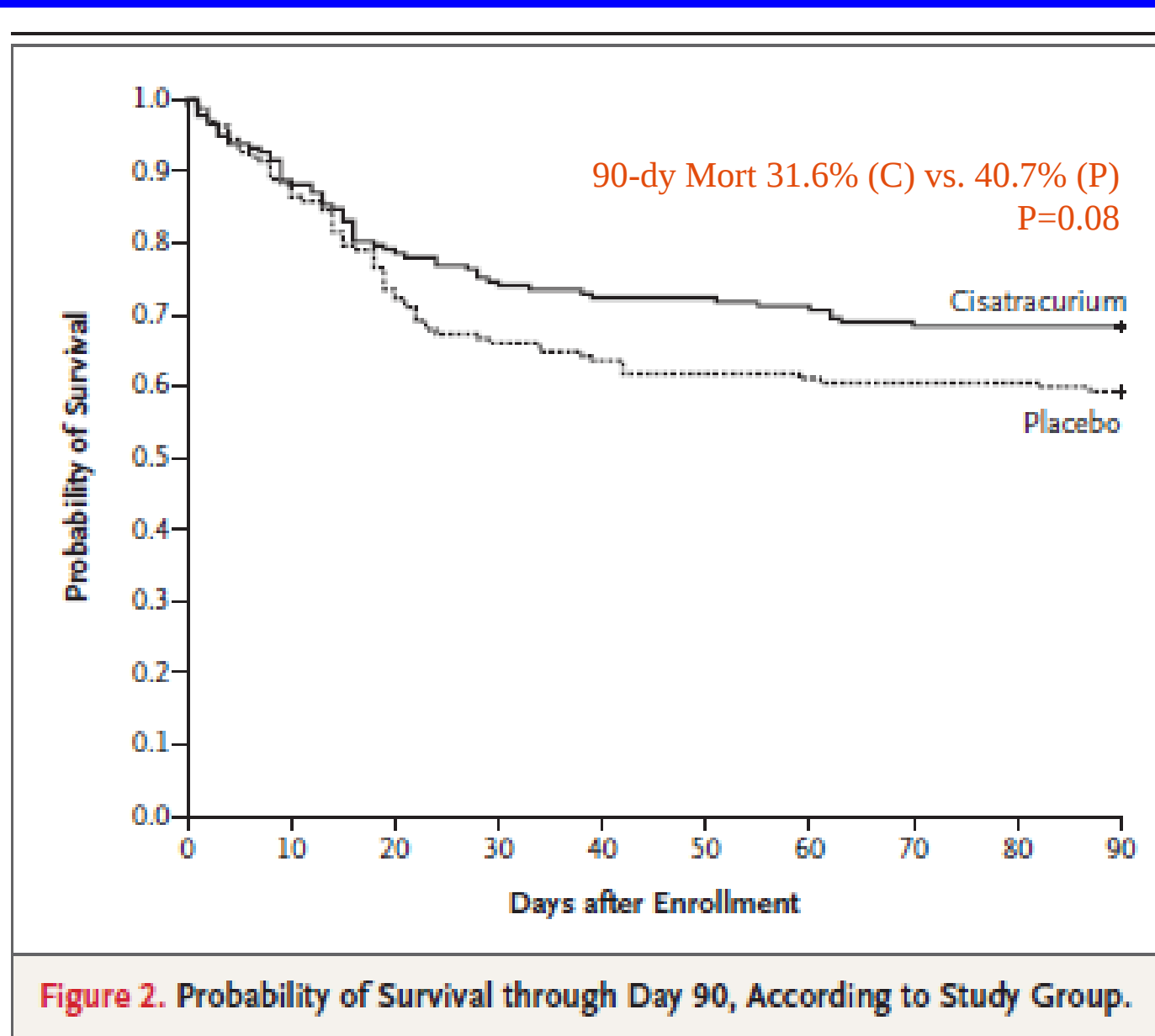
Papazian NEJM 2010

Neuromuscular Blockade
in ARDS

Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaél Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D.,
for the ACURASYS Study Investigators*

- ~170 patients per group (n=340), P/F <150 on A/C 6-8
- 20 ICUs in France
- Sedated (no specifics) to Ramsay 6 (no response)
- Blinded (asynchrony not monitored), Cisatracurium 15 mg bolus + 37.5 mg/hr gtt (with no T-o-F) vs. Saline
- Started ARDS day 1 and continued 48 hours
- Time-to-event survival at 90 days, HR=0.68 (0.48 to 0.98, p=0.04)
- Pneumothorax 11.7% placebo vs. 4.0% (p=0.01)



NMB vs. Placebo in ARDS*

Outcome	Relative Risk (not absolute reduction)	Quality of Evidence
28-day Mortality	~35% lower in NMB (+ sig)	Moderate
90-day Mortality	~25 lower in NMB (+/- sig)	Moderate
VFDs	~2 more VFDs in NMB	Moderate to High
ICU-acquired weakness	10% more risk (non-sig)	Poor
Barotrauma	~ 50% lower in NMB	Moderate

* analysis of data from 3 studies with ~430 patients from France by Papazian et al.

Papazian L et al, ACURASYS in NEJM 2010;363:1107-16

Forel JM and Papazian L, CCM 2006;34:2749-57

Gainnier M and Papazian L, CCM 2004;32:113-119

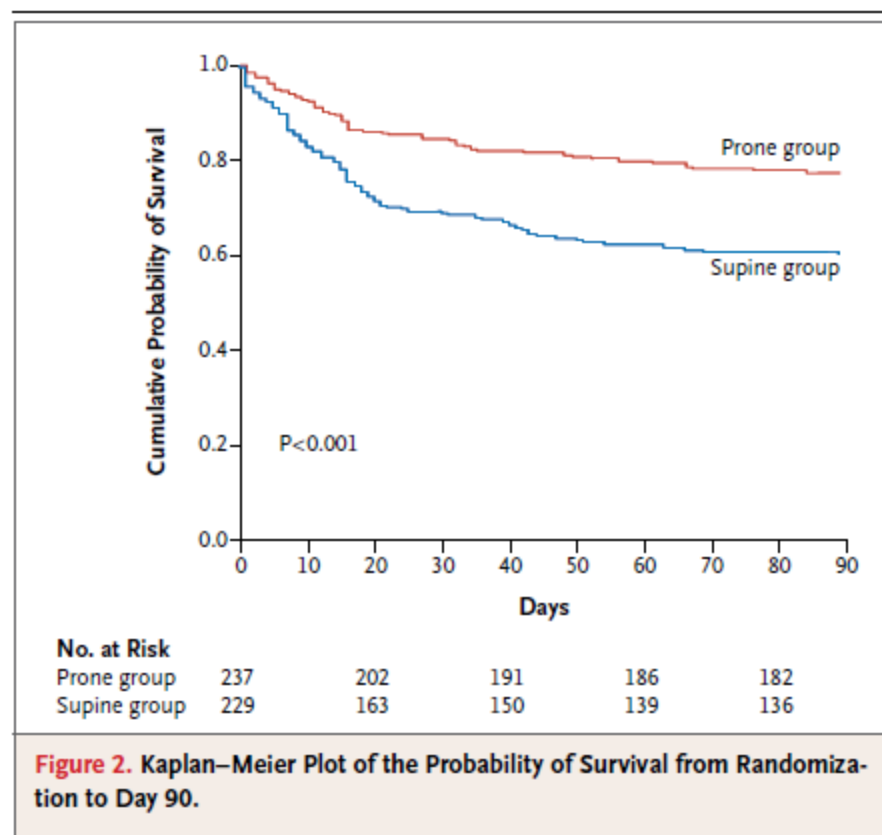
The NEW ENGLAND JOURNAL of MEDICINE

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JUNE 6, 2013

VOL. 368 NO. 23

Prone Positioning in Severe Acute Respiratory Distress Syndrome



Guerin C, NEJM
2013;368:2159-68

Prone Positioning – Evolution of Data

- Gattinoni L, NEJM 2001;345:568-73
 - No improved survival, too short time prone, and signal in severe
- Taccone P, JAMA 2009;302:1977-84
 - Triple risk of complications - increased sedation/NMB, airway obstruction, desaturation, vomiting, hypotension, lost IV access/ETT/Trac
- Guerin C, NEJM 2013;368:2159-68
 - N=466 in 27 French and 1 Spanish ICU
 - Severe ARDS (P/F <150 on 0.6) and >16 hours proning
 - 28-d mortality 16% prone vs. 33% supine (HR 0.39, p<0.001)
 - 90-d mortality 24% prone vs. 41% supine (HR 0.44, p<0.001)
 - Stopped proning when P/F $\geq$ 150 on PEEP $\leq$ 10 and FiO₂ $\leq$ 60%

OSCILLATION (HFO) NEGATIVE

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FEBRUARY 28, 2013

VOL. 368 NO. 9

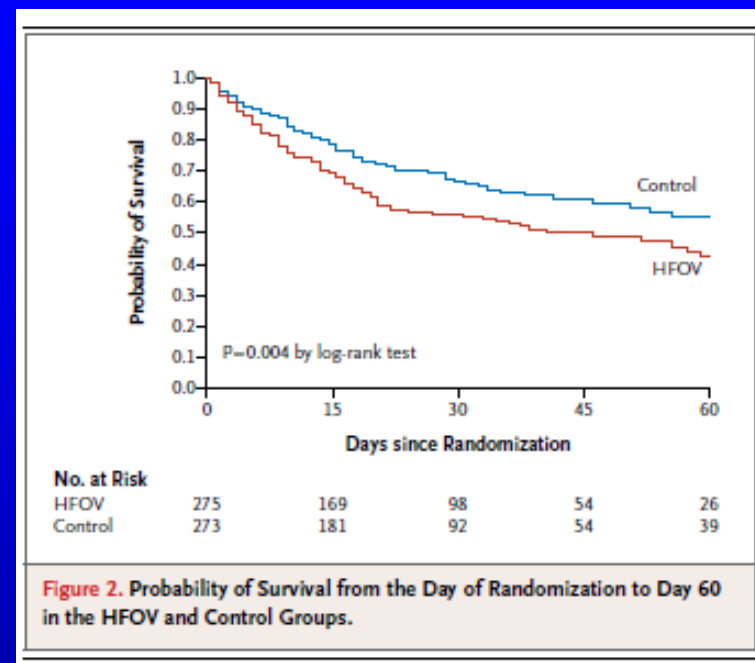
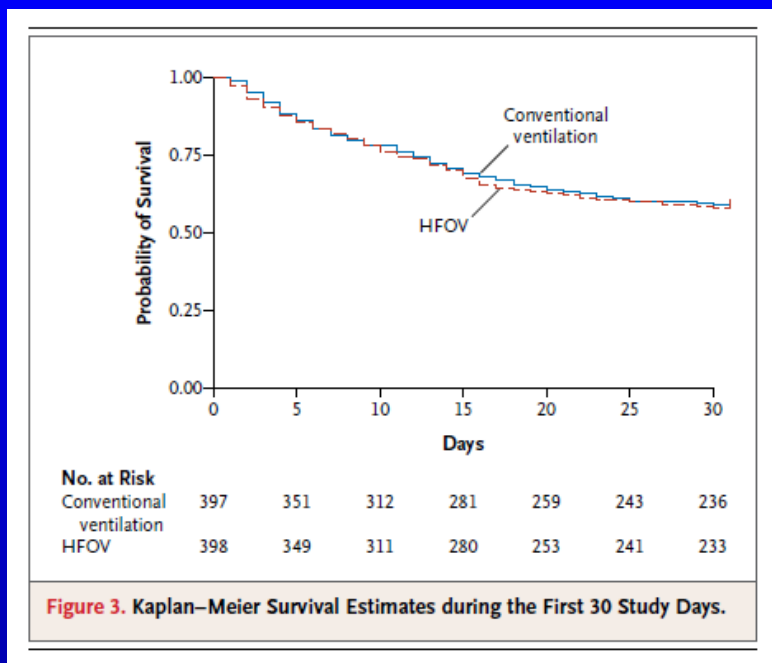
High-Frequency Oscillation in Early Acute Respiratory
Distress Syndrome

ORIGINAL ARTICLE

High-Frequency Oscillation for Acute
Respiratory Distress Syndrome

Duncan Young, D.M., Sarah E. Lamb, D.Phil., Sanjoy Shah, M.D.,
Iain MacKenzie, M.D., William Tunnicliffe, M.Sc., Ranjit Lall, Ph.D.,
Kathy Rowan, D.Phil., and Brian H. Cuthbertson, M.D.,
for the OSCAR Study Group*

OSCILLATION (HFO) NEGATIVE



- Despite “positive meta-analysis” (RR 0.77, 0.61-0.98, Sud S BMJ 2010), these two studies of patients with P/F <200 in n=800 and n=548 had mortality rates of 41% (OSCAR 30-d) and 47% HFO vs 35% controls (CCCTG hospital mortality)
- **Sedation and Paralysis use higher** in HFO groups (e.g., mean midaz 200/d)

Other aspects of Sepsis-induced ARDS management...

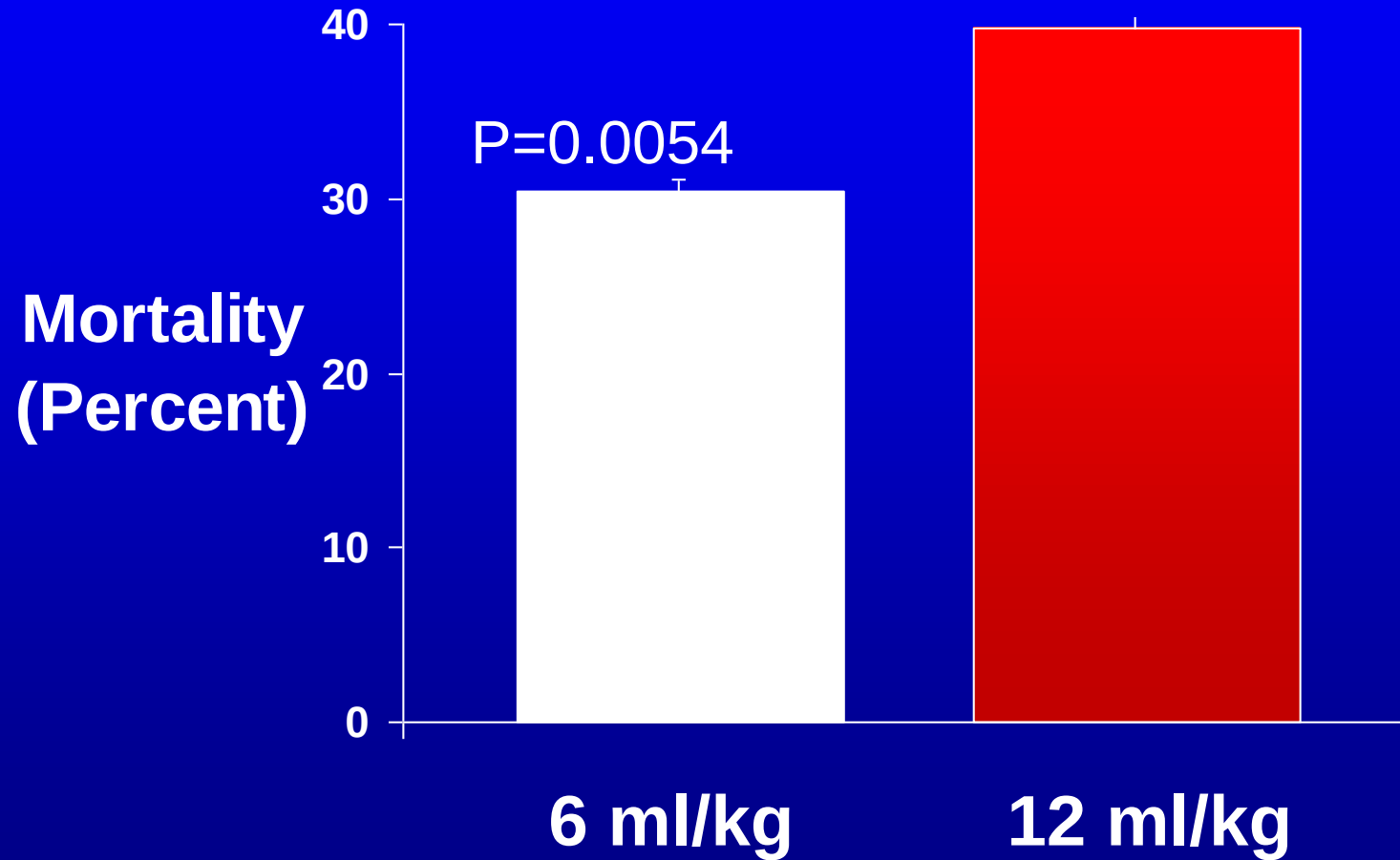
- Sedation and paralysis....
 - Weaning protocols with SBTs (grade 1)
 - Sedation protocols and minimization of sedation (grade 1)
 - Best way to minimize is with SATs (Kress NEJM, Girard, Lancet 2008)
- Still under study...
 - Prone positioning (grade 2)
 - Recruitment maneuvers (grade 2)
 - HFO (high frequency oscillation, OSCAR/OSCILLATE)
 - Routine neuromuscular blockade, NMB (grade ??)

NOTE: Problem is that these bottom Grade 2 choices may uproot plans for the top Grade 1 items

Bottom Line NMB, Proning, HFO

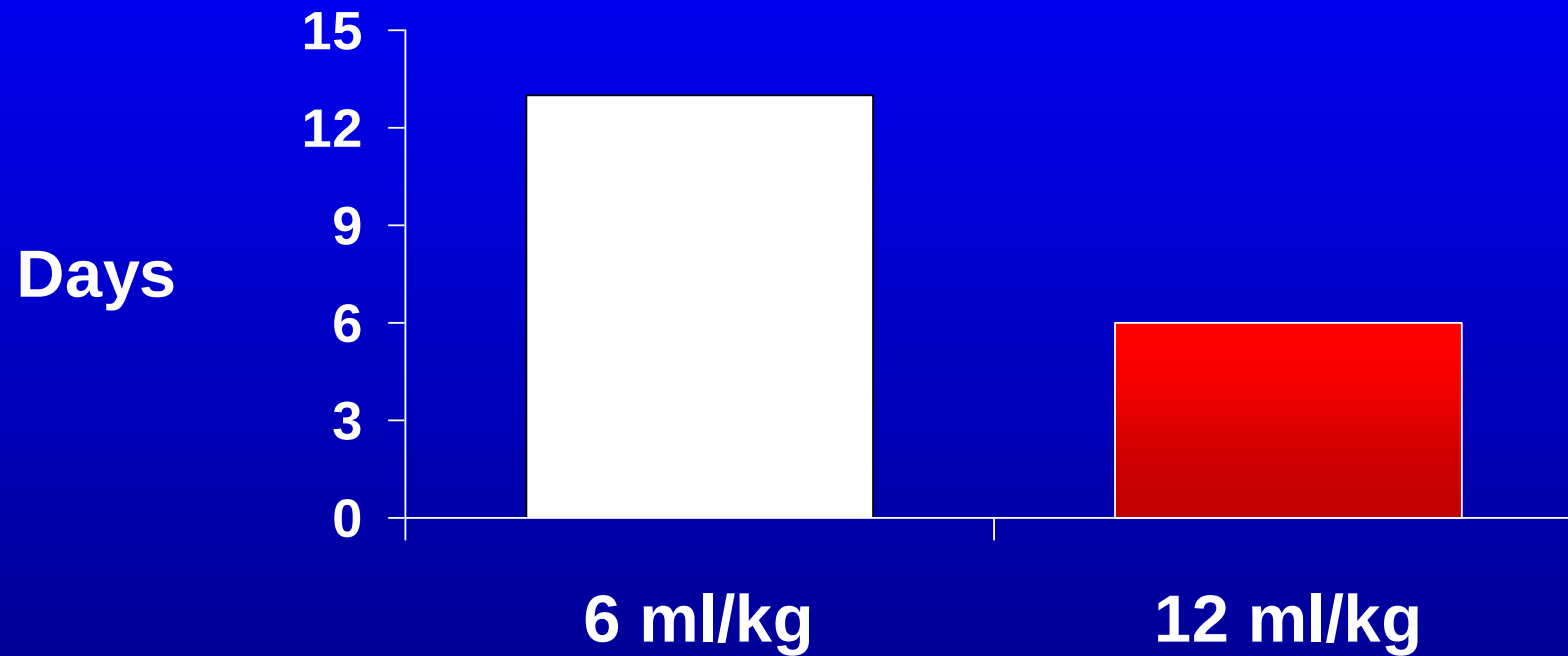
- Data don't support HFO and do support Proning only while deep P/F ratios present
- Proning thought to lessen VILI, overdistention, and by promoting recruitment (less lung stress and strain) – need skills (see video on NEJM website)
- Thus need NMB in rare patients for transient period, and be aware that NMB begets much more sedation and thus immobilization
- LIBERATION is better part of valor whenever able

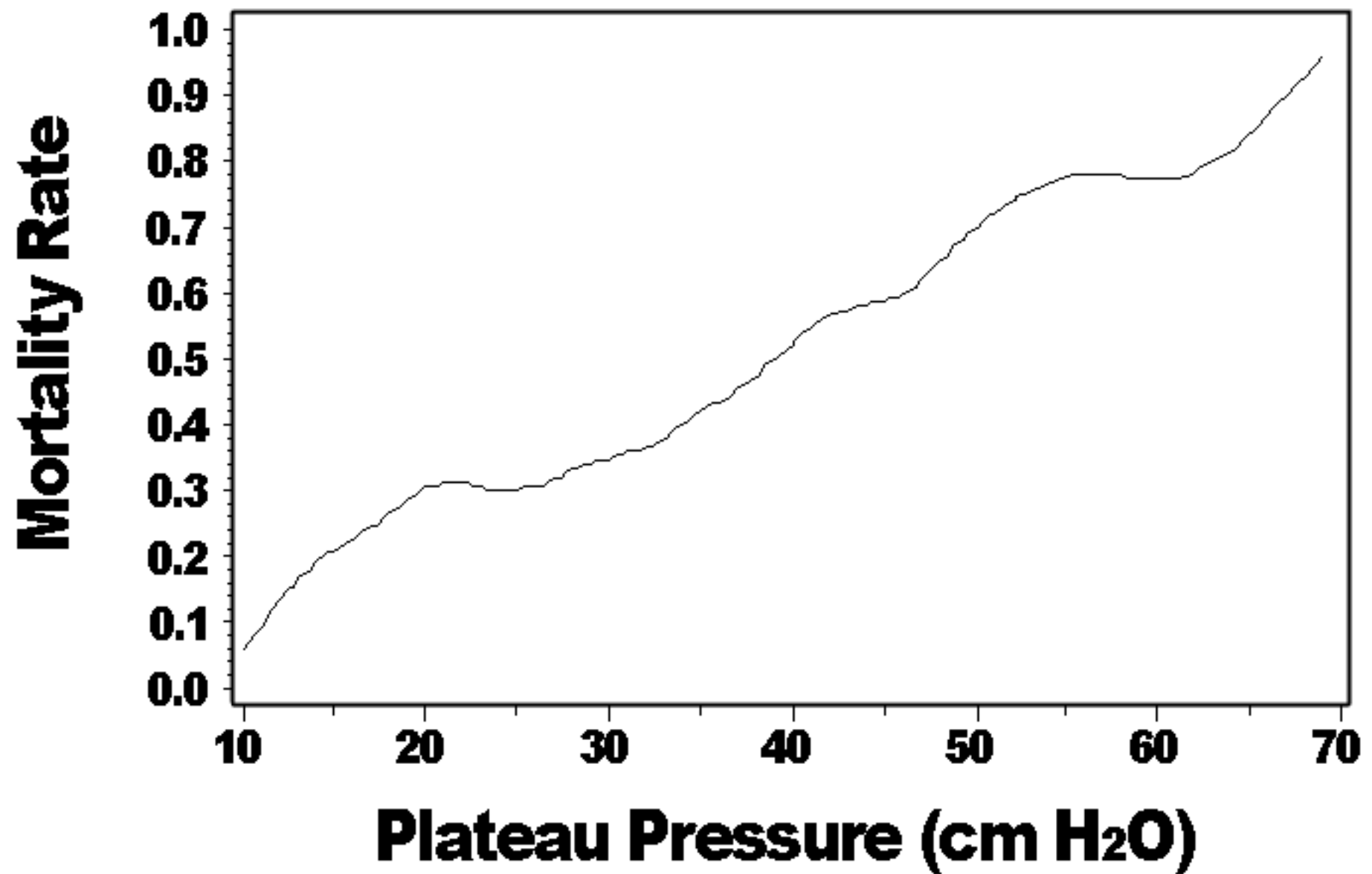
Mortality Prior to Hospital Discharge



ARDSnet, N Engl J Med 2000;342:1301-08

Median Ventilator-Free Days





Brower et al, AJRCCM 2002;166:1515-17

Brower et al, AJRCCM 2005;172:1241-5

Association Between Use of Lung-Protective Ventilation With Lower Tidal Volumes and Clinical Outcomes Among Patients Without Acute Respiratory Distress Syndrome

A Meta-analysis

Low Tidal Volumes for All?

Niall D. Ferguson, MD, MSc

along with the low specificity of the ARDS definition used,⁷ supports this notion because it is likely that substantial num-

20 articles, 2800 patients, NNT=11 for reduced lung injury development and **NNT=23 per life saved** (risk ratio 0.64, 0.46-0.89)

Neto AS, JAMA 2012;308:1651-59

Ferguson N, JAMA 2012;308:1689-90

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Higher versus Lower Positive End-Expiratory Pressures
in Patients with the Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute ARDS Clinical Trials Network*

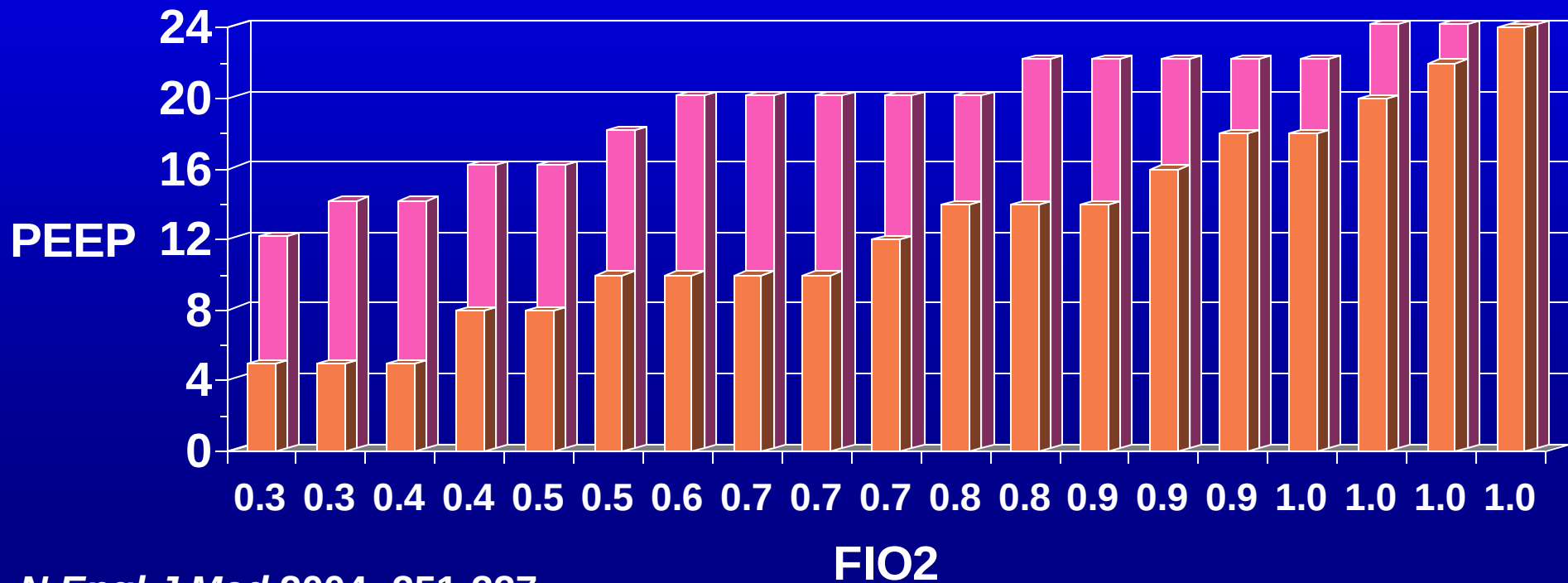
Hypothesis:

In patients with ALI ventilated with 6 mL/kg, higher levels of PEEP will result in better clinical outcomes than lower levels of PEEP.

N Engl J Med 2004; 351:327-336

Ventilation strategy

- All given 6 mL/kg PBW tidal volume
- Oxygenation: $\text{SpO}_2 = 88 - 95\%$ or $\text{PaO}_2 = 55 - 80$ mm Hg
- Standardized weaning



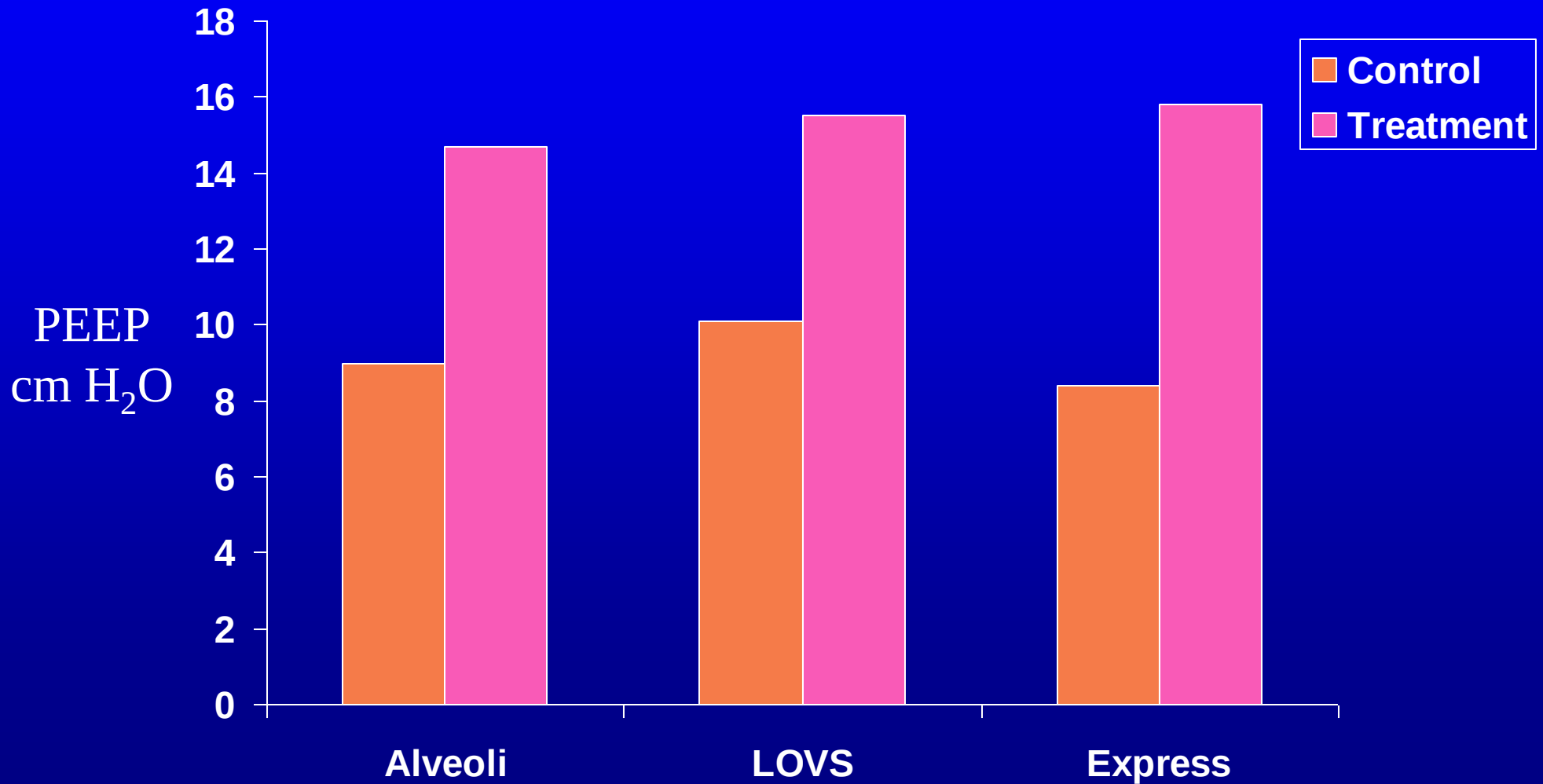
High versus Low PEEP in ALI

comments on next slide

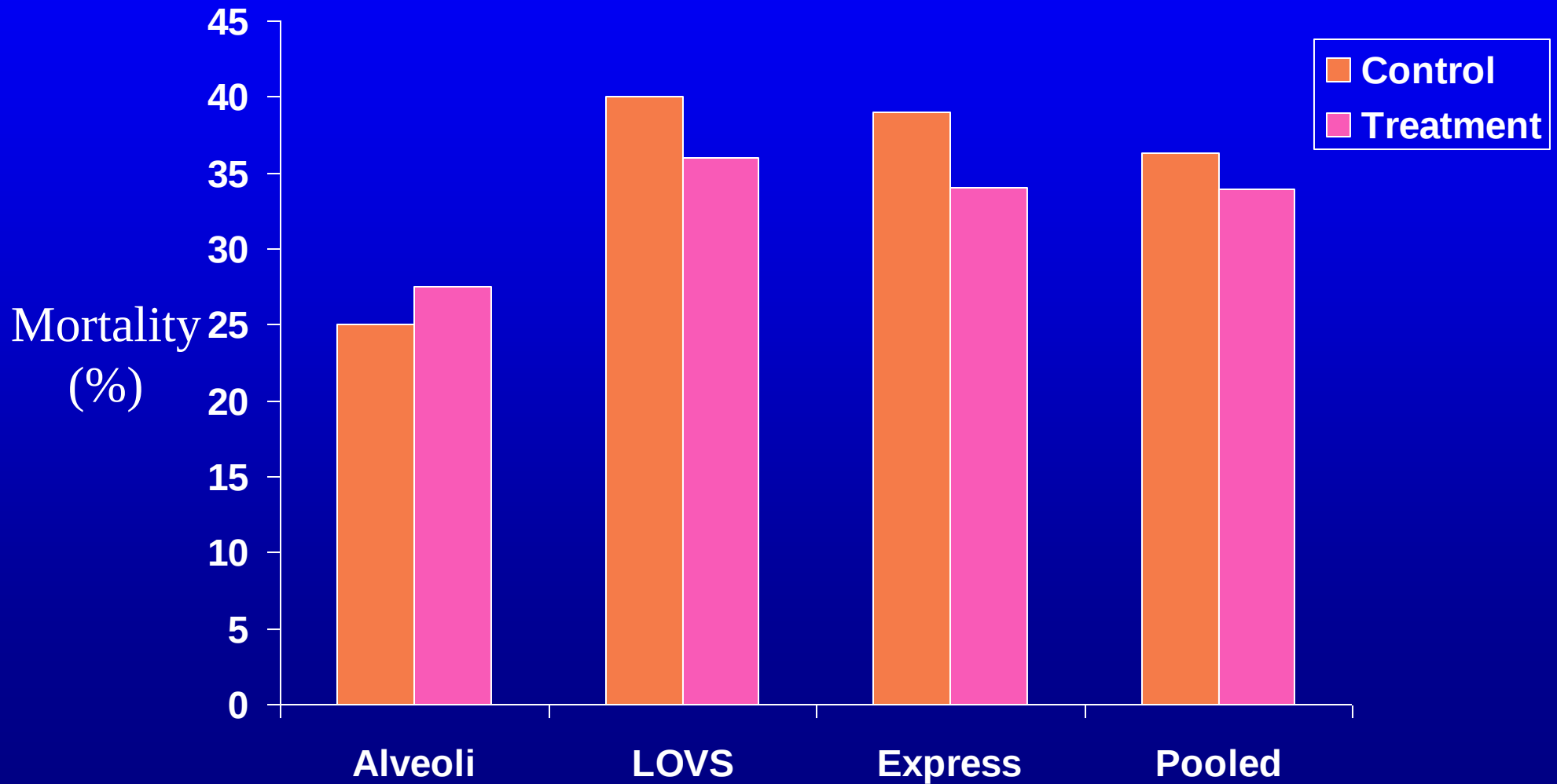
MAIN REFERENCES: (total n=2,299)

1. **ALVEOLI** USA NHLBI – used PEEP table and all Plt <30, age imbalance 49 vs. 54 yrs
2. **LOVS** Canadian CCTG – 6 yrs, 3 continents, 30 hospitals, used PEEP table w/ Plt P <30 vs. Plt P <40
3. **EXPRESS** French – 37 ICUs, all get 6ml/kg, control PEEP 5 to 9 vs. treatment PEEP increased to keep Plt P 28-30
4. Meta-analysis (Briel M et al) – Higher PEEP was not associated with improved survival except for the subgroup with ARDS
 1. **NEJM** 2004; 351:327-336, n~550
 2. **JAMA** 2008;299:637-45, n~980
 3. **JAMA** 2008;299:646-55, n~770
 4. **JAMA**, 2010;303:865-73, n=2,299

PEEP Level Tested (day 1 values)



28-Day Mortality Rates



LOVS Canadian Trial of Alveolar Recruitment:

Table 5. Cointerventions During the First 28 Days of Study^a

Cointerventions	Lung Open Ventilation	Control Ventilation
Sedative infusion	423 (89.1)	457 (90.0)
Days of sedative infusion, median (IQR)	7 (3-12)	7 (4-12)
Sedative or narcotic infusion	449 (94.5)	476 (93.7)
Days of sedative or narcotic infusion, median (IQR)	7 (4-13)	8 (5-14)
Neuromuscular blockade	208 (43.8)	223 (43.9)
Days of neuromuscular blocker use, median (IQR)	2 (1-5)	3 (1-6)
Vasopressors	339 (71.4)	377 (74.2)
Days of vasopressor use, median (IQR)	4 (2-8)	5 (2-9)
No. of vasopressors each day in use, median (IQR)	5 (3-10)	6 (3-12)
Pulmonary artery catheter	164 (34.5)	180 (35.4)
Corticosteroids	194 (40.8)	216 (42.5)
Hemodialysis ^b	71 (16.6)	85 (18.5)

Meade M, JAMA 2008;299:637-45

EXPRESS French Trial of PEEP for Alveolar Recruitment:

Table 5. Cointerventions and Adjunctive Therapies

Intervention	No. (%) ^a		<i>P</i> Value
	Minimal Distension (n=382)	Increased Recruitment (n=385)	
During the first 72 h			
Fluid loading	255 (66.8)	290 (75.3)	.01
Volume of fluids, median (IQR), L ^b	0.5 (0-1.5)	1.0 (0.1-2.2)	<.001
During the first 7 d			
Epinephrine or norepinephrine	286 (74.9)	289 (75.1)	.95
Corticosteroids	198 (51.8)	199 (51.7)	.97
Neuromuscular blockade	209 (54.7)	204 (53)	.63
Recruitment maneuvers	49 (12.8)	27 (7.0)	.007
Adjunctive therapies during the first 7 d			
Prone position	72 (18.8)	34 (8.8)	<.001
Inhaled nitric oxide	98 (25.7)	57 (14.8)	<.001
Almitrine bismesylate	25 (6.5)	14 (3.6)	.07
Any therapy	132 (34.6)	72 (18.7)	<.001
Mortality in patients who received rescue therapy	62 (47.0)	37 (51.4)	.55

Abbreviation: IQR, interquartile range.

^aUnless otherwise indicated.

^bTotal volume of colloids and/or crystalloids given as bolus injections.

High vs. Low PEEP

Outcomes of recent trials

- **Important:** All 3 studies negative for mortality outcome
- **Interesting:** Survival better in high PEEP subgroup w/ARDS vs survival worse in patients w/ALI
- In all 3, sepsis was main diagnosis leading to ARDS (65%, 90%, 85%)
- Weaning protocols = no f/Vt screening, prompts to MDs on successful pass of 2-hr SBTs
- LOVS reported 95% on sedatives & narcotics for 7 days

1. NEJM 2004; 351:327-336
2. JAMA 2008;299:637-45
3. JAMA 2008;299:646-55
4. JAMA, 2010;303:865-73, n=2,299

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

ESTABLISHED IN 1812

APRIL 20, 2006

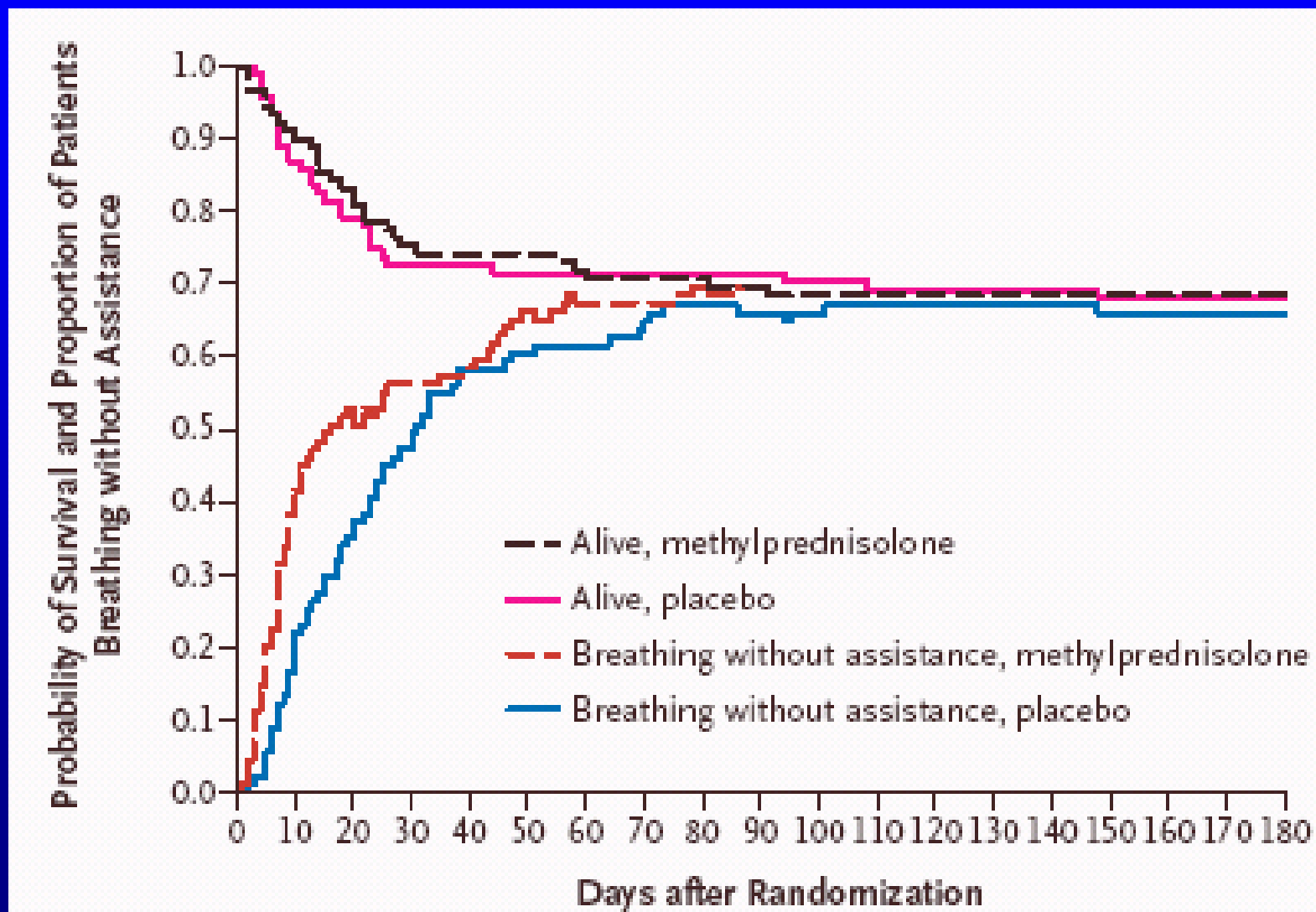
VOL. 354 NO. 16

Efficacy and Safety of Corticosteroids for Persistent Acute
Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS)
Clinical Trials Network*

- Randomized, blinded controlled trial of methylprednisilone vs. placebo for ALI persisting > 7 days
 - 2 mg/kg/day x 14 days; then 1 mg/kg/day x 7 days then tapered over 4 days.

Methylprednisilone vs. placebo results



The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MAY 25, 2006

VOL. 354 NO. 21

Pulmonary-Artery versus Central Venous Catheter to Guide
Treatment of Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome
(ARDS) Clinical Trials Network*

FACTT: Factorial trial design

Fluid Management

C
A
T
H
E
T
E
R

PAC
(n = 500)

CVC
(n = 500)

“Conservative”
(n = 500)

“Liberal”
(n = 500)

250 patients

250 patients

250 patients

250 patients

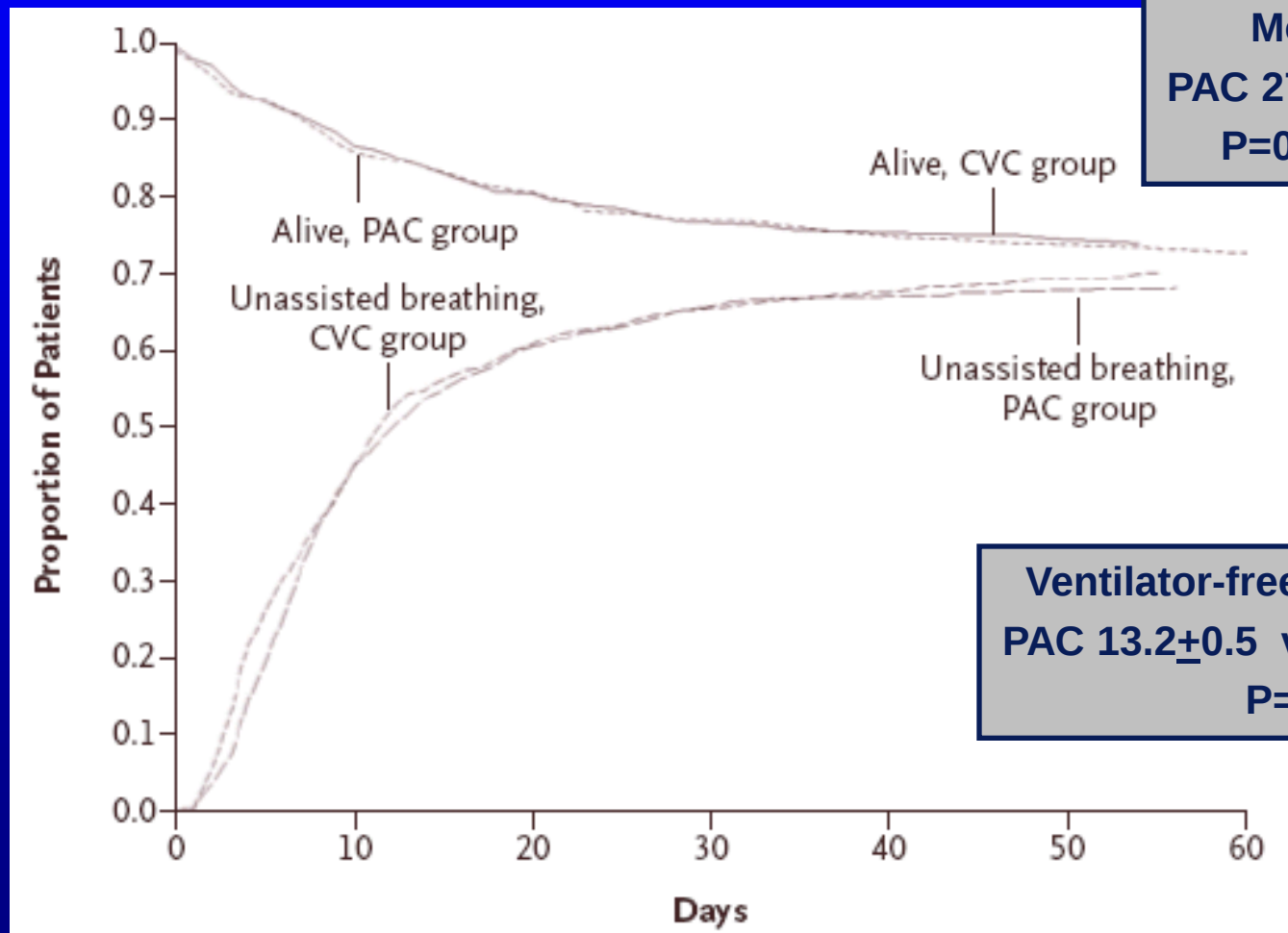
Acceptable MAP off vasopressors

Intravascular Pressure (PAOP/CVP)	Low MAP	Low UOP		Acceptable UOP	
		low flow	nl flow	low flow	nl flow
>> Normal	Vasopressor Fluids	Dobutamine Lasix	Lasix	Dobutamine Lasix	Lasix
> Normal		Dobutamine	Lasix	Dobutamine	Lasix
High normal		Fluid	Fluid	Fluid	Cons. Lasix
Low normal		Fluid	Fluid	Fluid	Liberal Fluid

No differences between PAC and CVC in:

- Blood pressure
- Heart rate
- CVP
- Net fluid balance
- Vasopressor use
- Tidal volume
- PEEP
- Plateau pressure
- Oxygenation measures

Kaplan Meier estimates of survival and unassisted breathing



Mortality to day 60
PAC 27.4% vs. CVC 26.3%
P=0.69 CI -4.4 to 6.6%

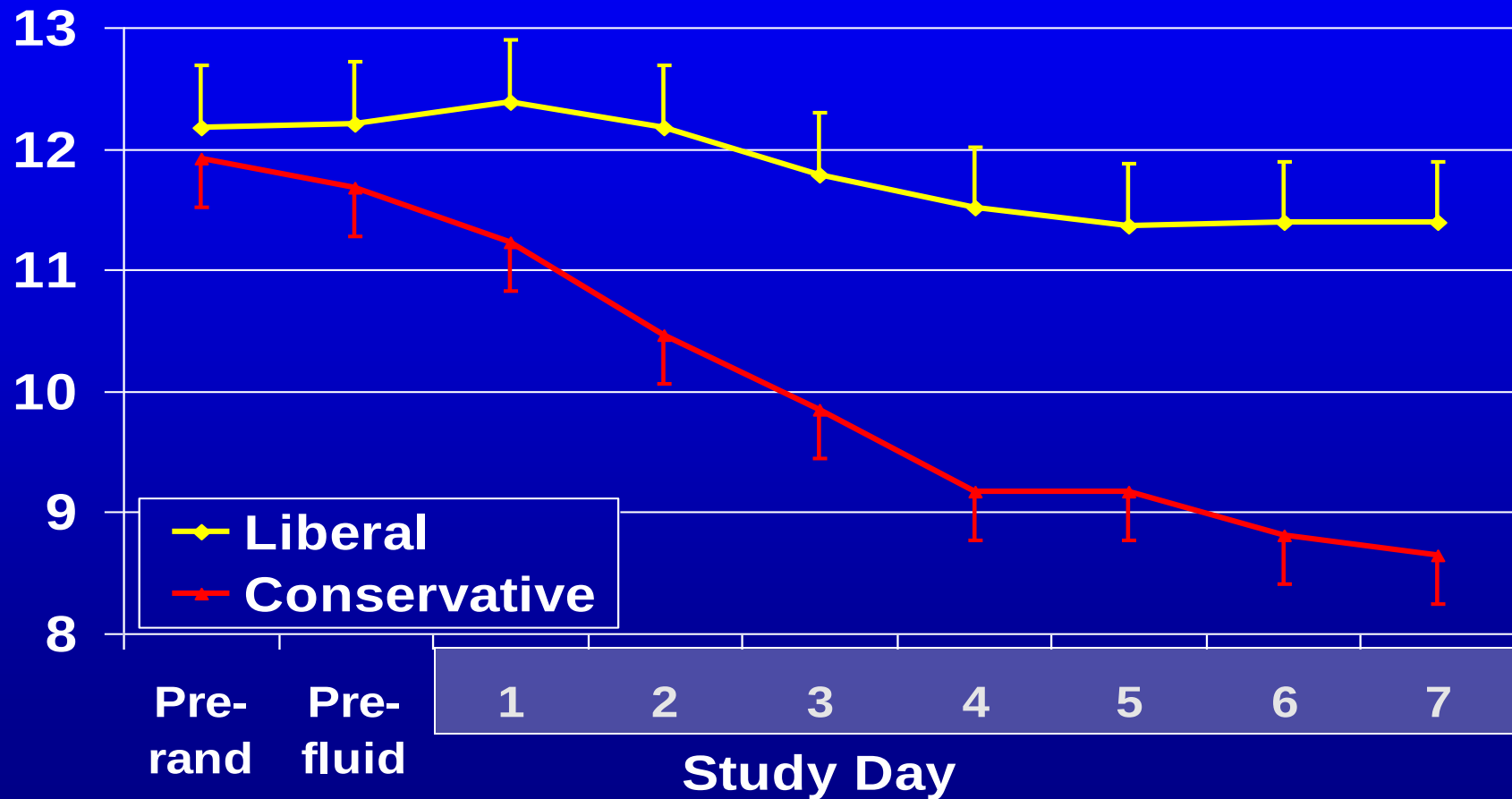
Ventilator-free days to day 28
PAC 13.2±0.5 vs. CVC 13.5±0.5
P=0.58

ORIGINAL ARTICLE

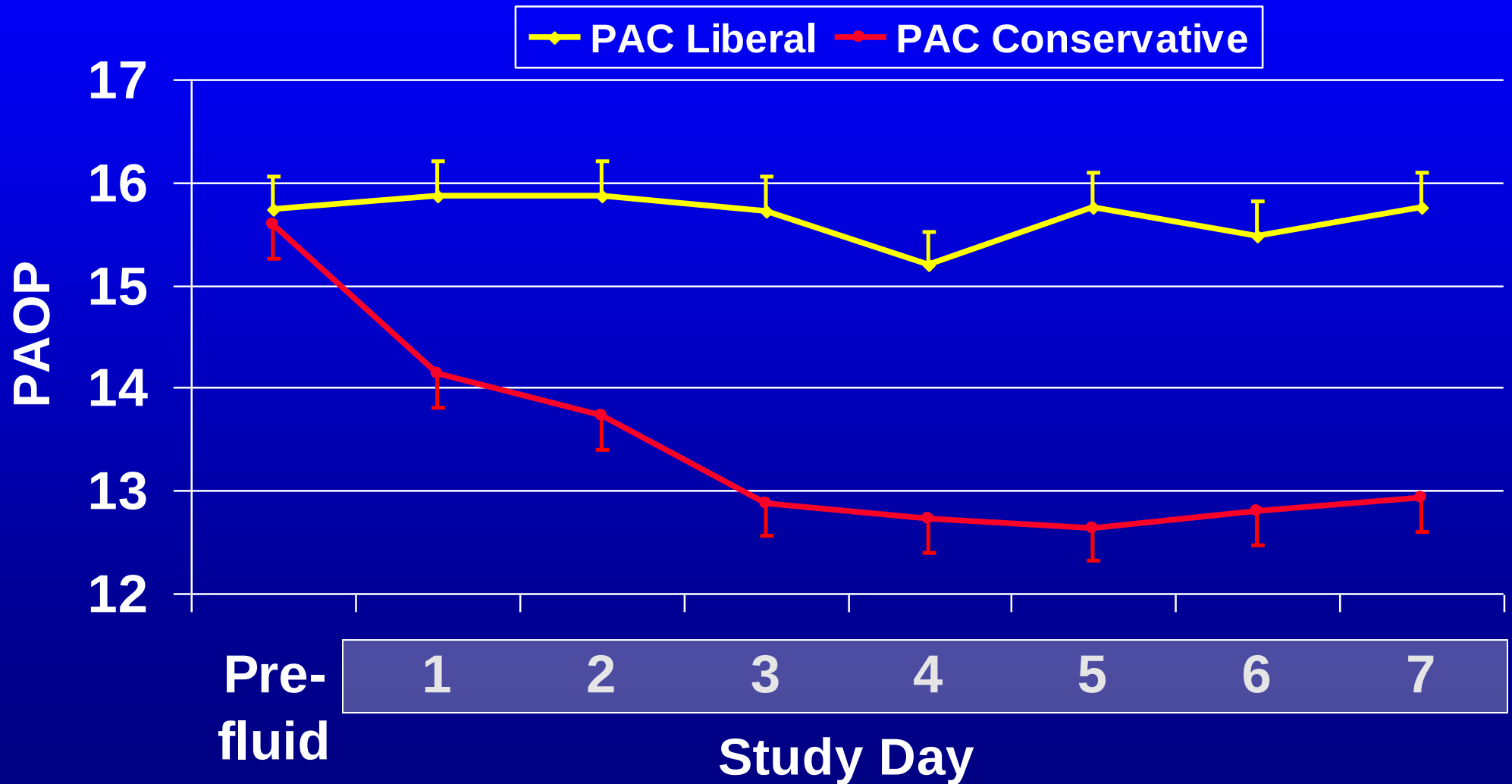
Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

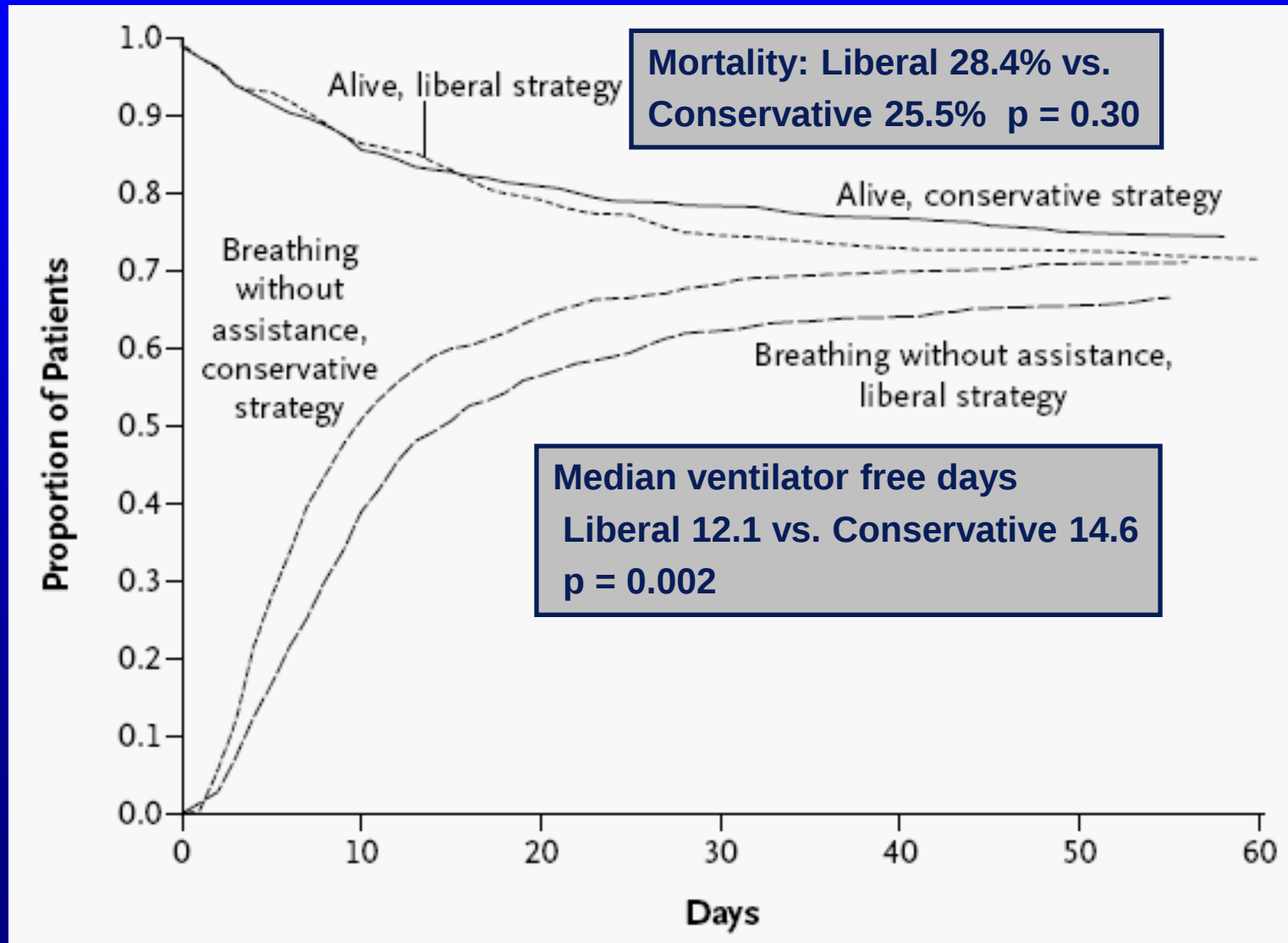
CVP separation



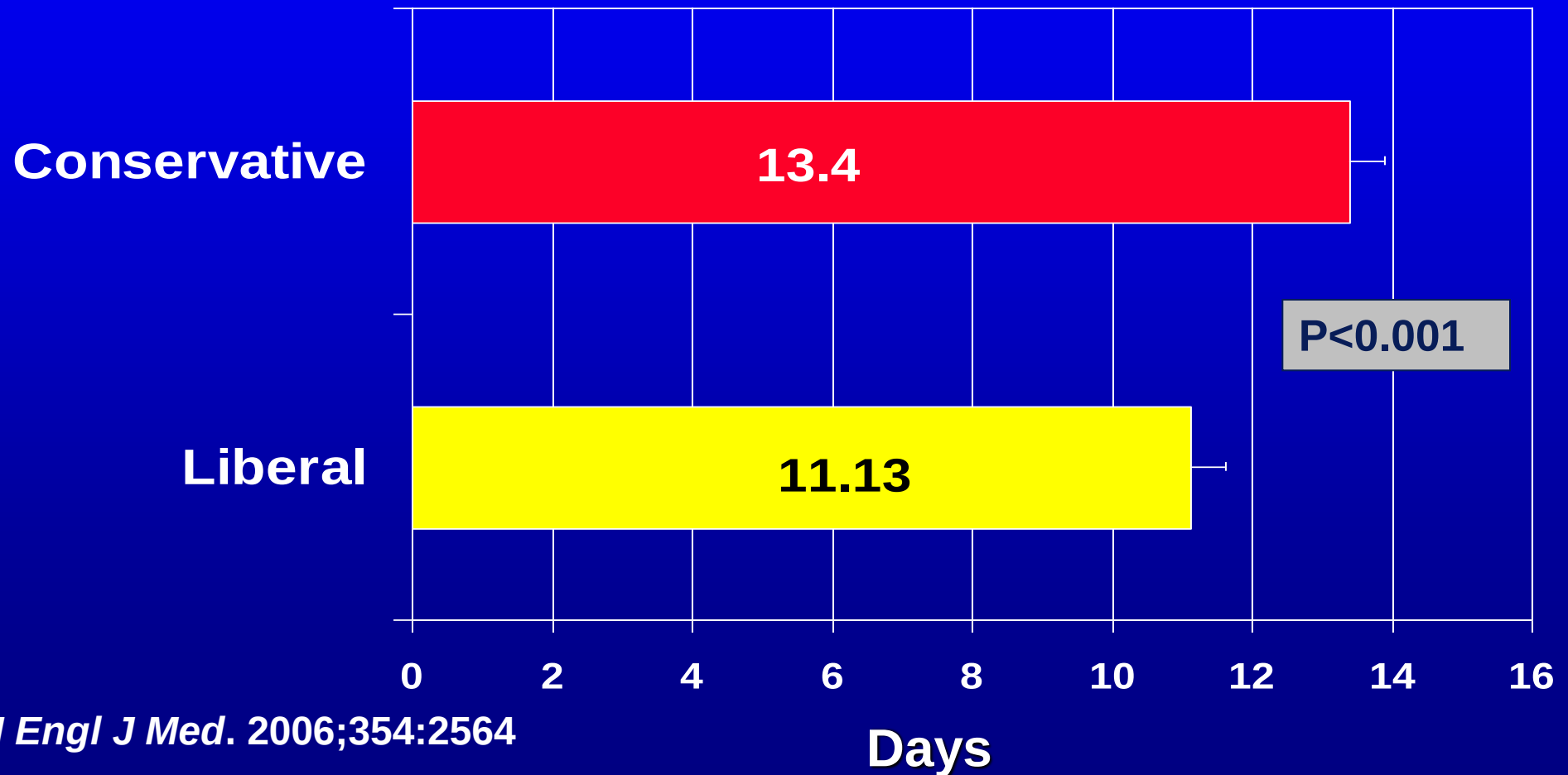
PAOP separation



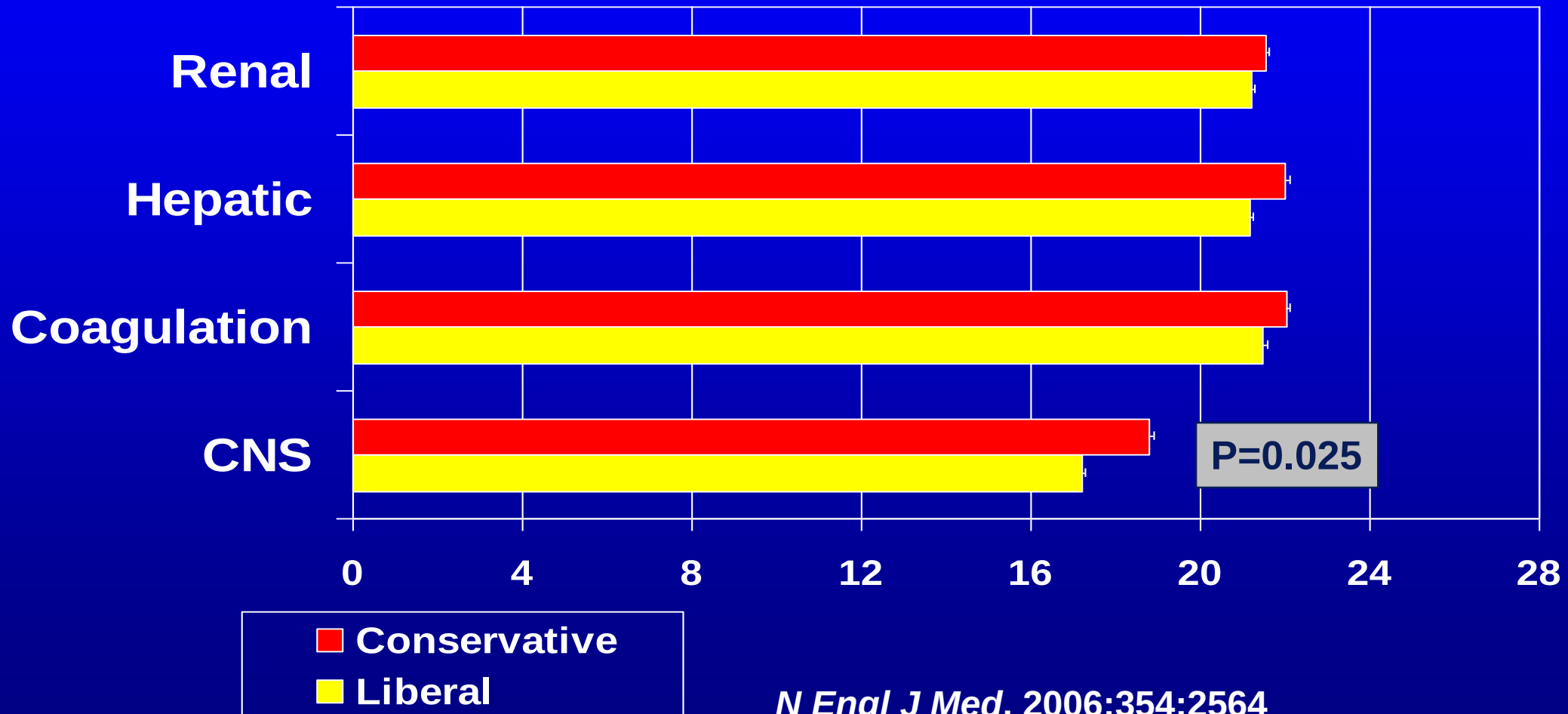
Survival to hospital discharge and breathing without assistance to day 60



ICU free days to day 28



Organ failure free days to day 28



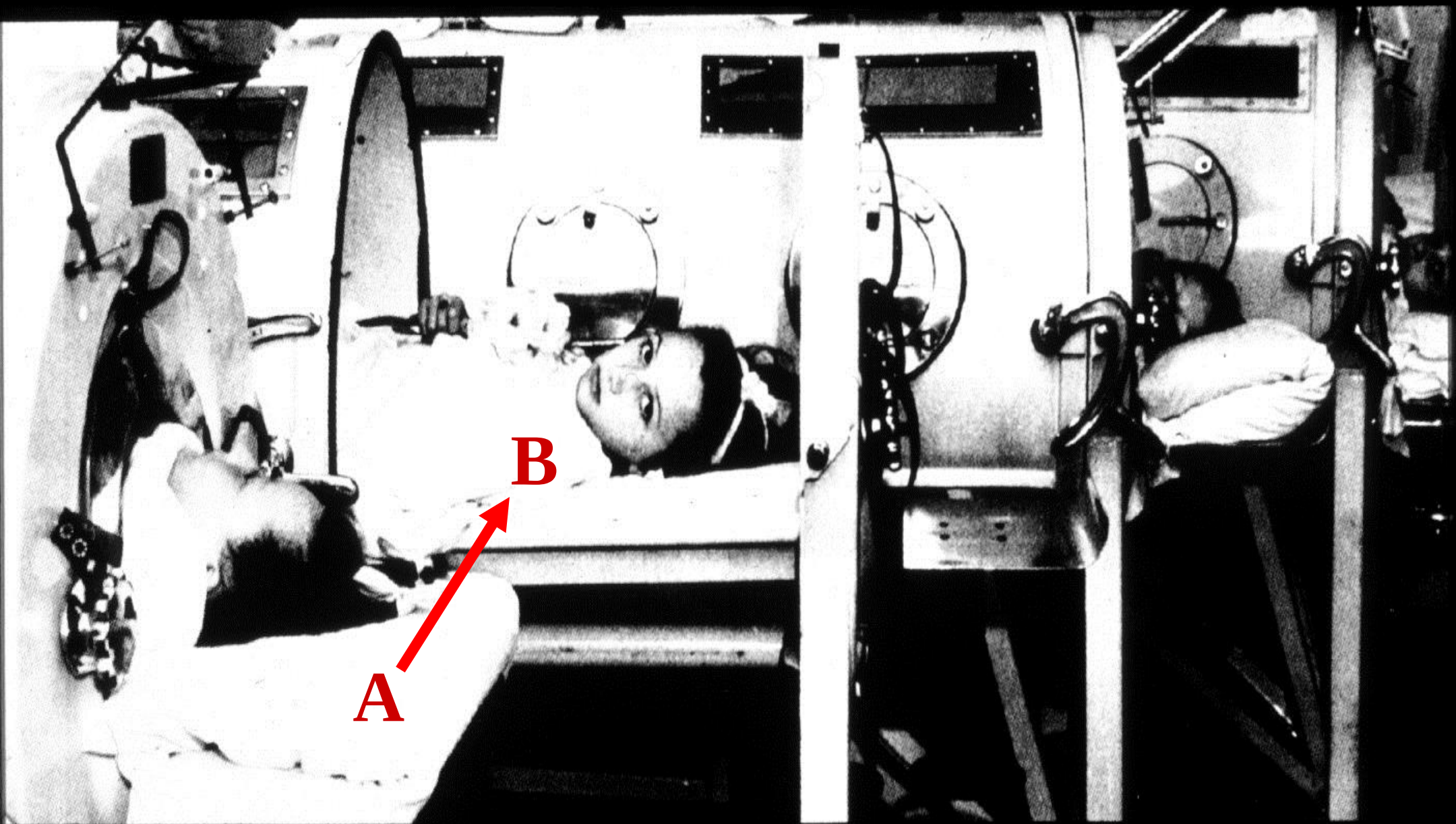
Conclusions on Management of ALI

- Use a normal tidal volume
- Use a level of PEEP you like
- Corticosteroids improve oxygenation not survival
- Routine use of a PAC should be avoided
- Application of a fluid conservative protocol after shock resolution improves physiology and shortens time on ventilator

Sedation and Weaning Protocols



(these slides included for completeness yet due to time limitations, this topic will be covered in a subsequent lecture)



“Scientific” Advance...

Science is knowledge,
based on observed facts and tested truths,
arranged in an orderly system.

Protocols are a “Scientific” Advance...

...when derived from knowledge,
based on observed facts and tested truths,
arranged in an orderly system.

Pigs can't fly



Why pigs can't fly

PIGS

- Heavy
- Minimal thrust
- No lift capability
- Limited control



BIRDS

- Light
- Adequate thrust
- Good lift
- Excellent control

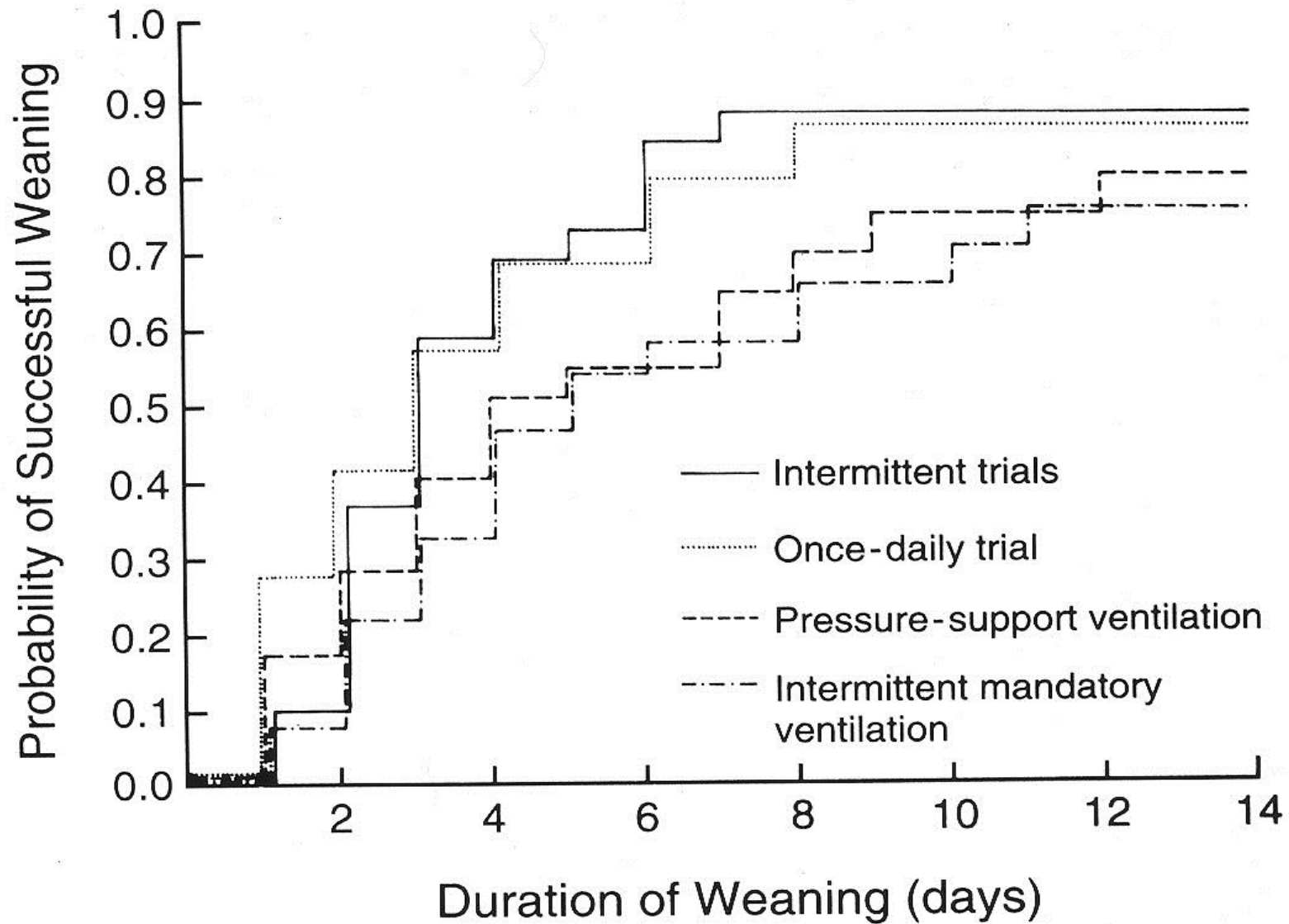
Every system is perfectly designed to achieve the results that it yields.

Structure & organization of ICU care *is at least as important as technology*

- Offer greater opportunities to improve outcomes than do technical innovations (e.g., airline industry)
- Pareto principle: 80-85% of opportunities to improve relate to flaws in systems that hinder individuals' ability to do their jobs well
- Clinical Protocols in mechanical ventilation supported by ABIM trainees and examination results
- At the same time, having checklist / protocol on paper is not good enough. You have to use it!

Prasad M et al, JAMA 2011;306:935-41

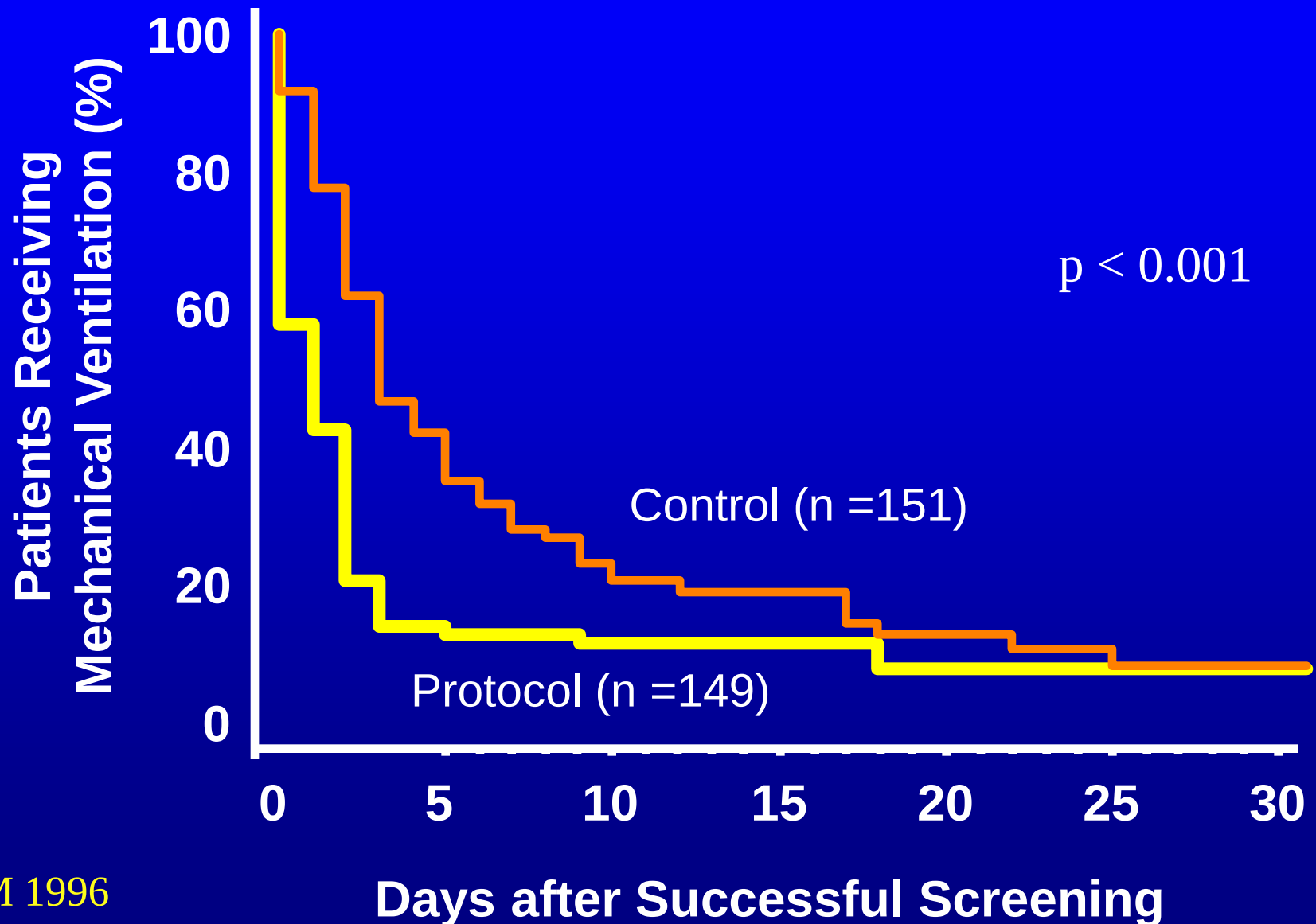
Weiss C et al, AJRCCM 2011;184:680-86



Esteban et al, NEJM 1995;332:345-50

Outcomes

Protocol group off ventilator earlier



Issues to consider

- All of the managing physicians were aware that T-pieces were superior to other modes in Esteban trial
- They knew the elements of the study and told us that the protocol wouldn't improve outcomes
- All groups had balanced modes of mechanical ventilation at enrollment and the option for daily SBTs

Outcomes of 1st PRCT of Weaning Protocol vs. Control

	Intervention n=149	Control n=151	P-value
APACHE II	19.8	17.9	0.01
Weaning Days	1	3	0.0001
Ventilator Days	4.5	6	0.003
Reintubation (%)	6 (4)	15 (10)	0.04
Mech Vent >21d (%)	9 (6)	20 (13)	0.04
Any Complication(%)	30 (20)	62 (41)	0.001
Total ICU Costs	\$15,740	\$20,890	0.03

Why did that happen?

- Good doctors and therapists don't always do what they know to be right.
- Context and time matter more than what we know to be right
- Comments from The Tipping Point by Malcolm Gladwell

EVIDENCE-BASED WEANING GUIDELINES

- Weaning Protocols for Non-Physician Health Care Professionals
- 7 major points based on available literature...
- Primarily **level I evidence, grade A recs**
(2 or more randomized controlled trials)

MacIntyre NR et al., *Chest* 2001;120:375S-395S
Ely EW et al., *Chest* 2001;120:454S-463S

Master Document
Protocol Summary

2013 Surviving Sepsis Guidelines

- Weaning and Sedation Protocols -

- SATs - Use sedation protocols with sedation goal and either intermittent sedation or continuous infusion with daily interruption or lightening (Grade 1)
- SBTs - Use a weaning protocol and SBTs regularly to evaluate the potential for discontinuing mechanical ventilation (Grade 1)

Dellinger P et al, Intensive Care Med 2008

Dellinger P et al, CCM 2013

Narrowing the bell curve *using Protocols*

In any process, reducing variability in that process inevitably leads to greater efficiency and lower cost.

W. Edwards Deming
1900-1993



More disarray = more help from protocols

Likewise

Less disarray = less margin for improvement

Protocols are not a
“one shoe fits all” construct

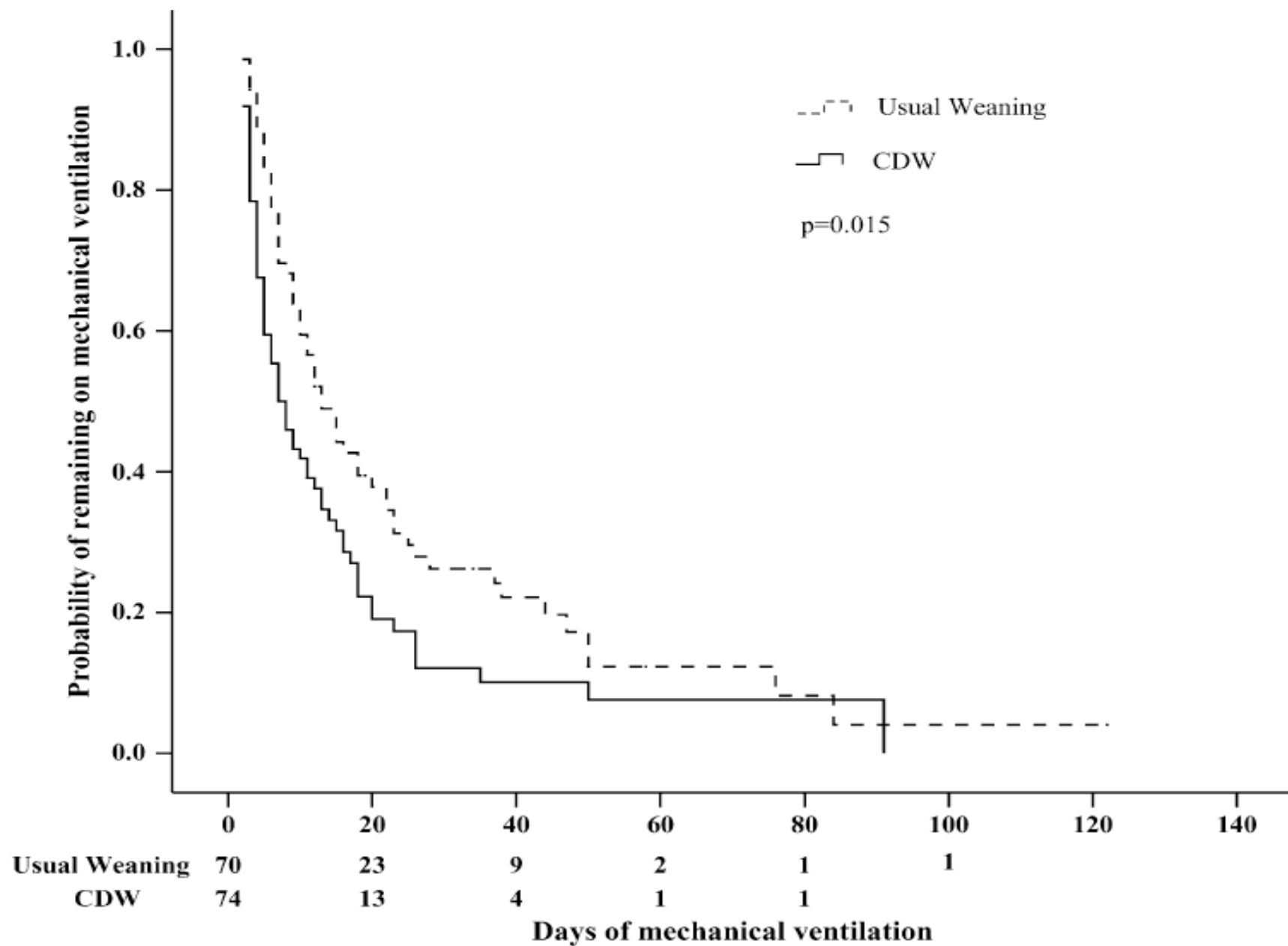
Protocols are not “cook-book” medicine

A Multicenter Randomized Trial of Computer-driven Protocolized Weaning from Mechanical Ventilation

François Lellouche, Jordi Mancebo, Philippe Jolliet, Jean Roeseler, Frédérique Schortgen, Michel Dojat, Belen Cabello, Lila Bouadma, Pablo Rodriguez, Salvatore Maggiore, Marc Reynaert, Stefan Mersmann, and Laurent Brochard

- 5 University Hospital ICUs (France, Spain, Belgium, Switzerland)
- Physician-controlled vs. Computer-driven weaning with mandated SBT and PROMPT
- N=144 pts
- Liberalized criteria
 - no f/V_t
 - go to SBT if PSV <8 and FiO₂ <50%

Lellouche et al, AJRCCM 2006,174:894-900



2 Miscellaneous but Important Issues in Weaning

1. Noninvasive Positive Pressure Ventilation
2. Tracheostomy

What is the evidence for/against
noninvasive positive pressure ventilation
(NIV)?

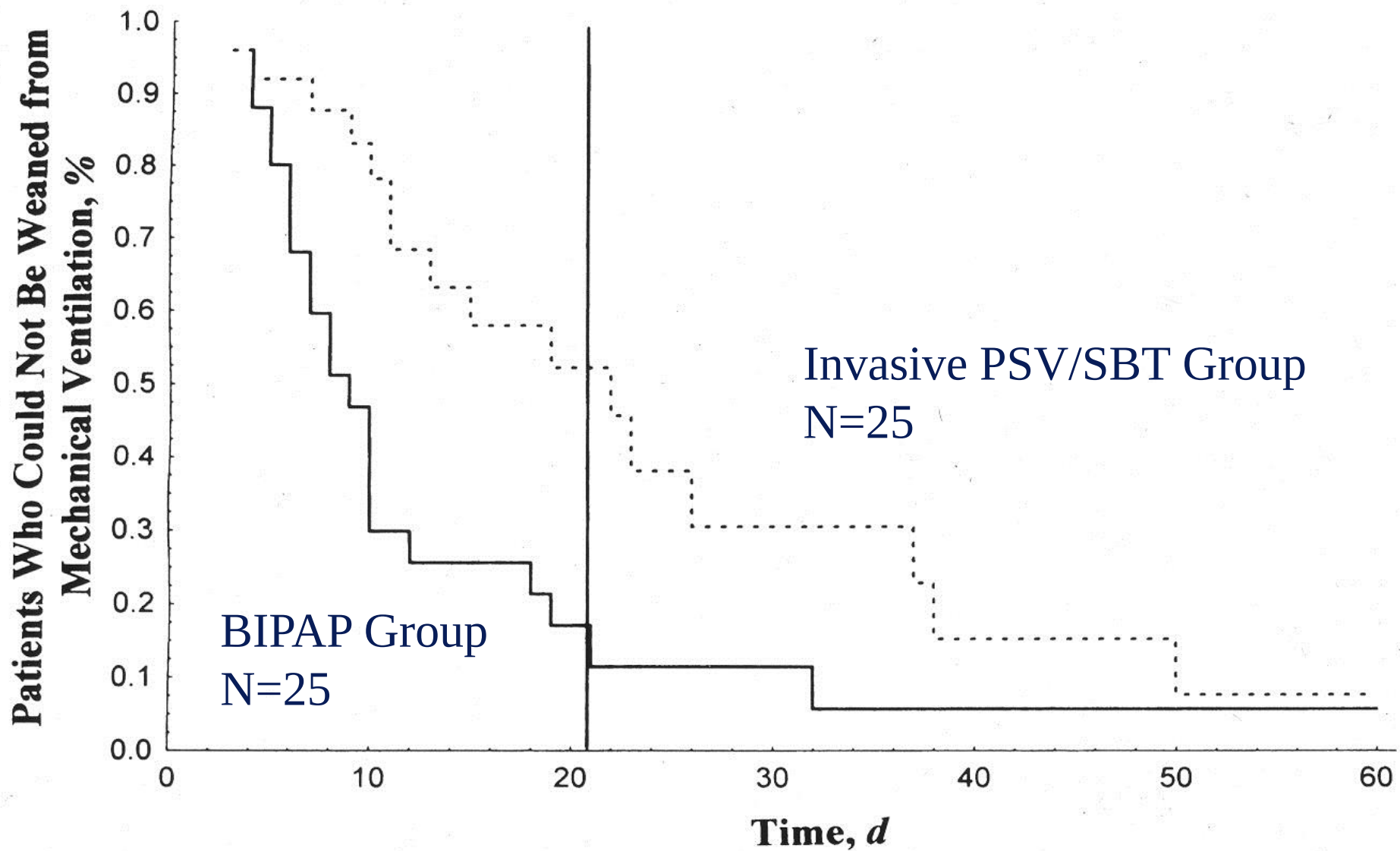
(a) weaning

(b) post extubation respiratory distress

Nava et al, Ann Intern Med 1998;128:721-728

Girault C, AJRCCM 1999;160:86-92

Girault C, AJRCCM 2011;184:672-79



Nava et al, Ann Intern Med 1998;128:721-728
Girault C, AJRCCM 1999;160:86-92

Randomized Trial in MICU Patients Failing SBT for 3 days

Outcome	NIV (n=21)	SBTs (n=22)
Intubation (d)	9.5	20.1
Vent Support (d)	11.4	20.1
ICU LOS (d)	14.1	25.0
LOS Hospital (d)	27.8	40.8
Complications	24%	73%
ICU Survival	90%	59%

Ferrer M, AJRCCM 2003;168:70-76.

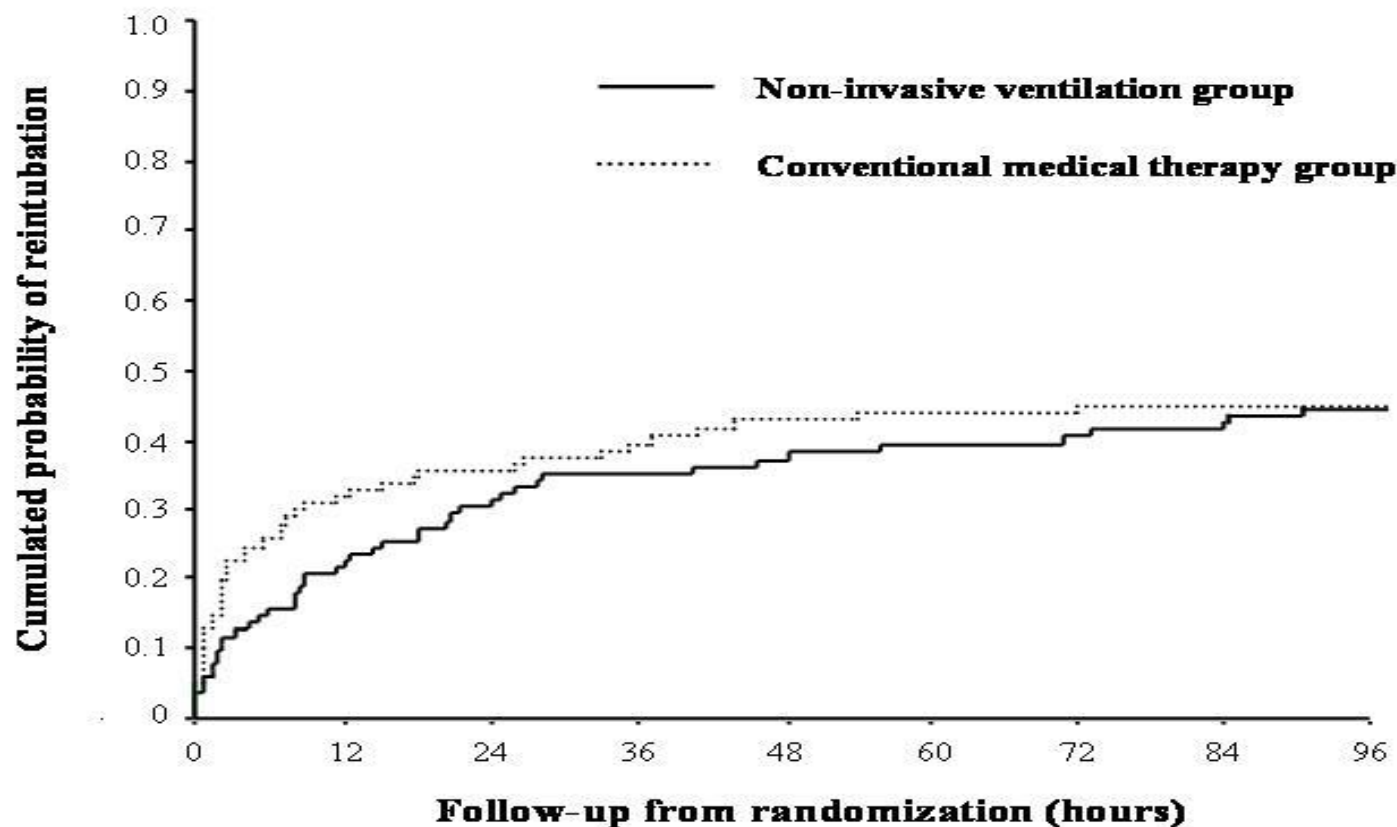
note: chronic disease, APACHE of 18, enrolled on day 7, more sedation in SBT arm

NIV for Post-Extubation Respiratory Distress

- RCT of 81 patients with >2 days of mechanical ventilation and respiratory distress within 48 hours of extubation
- NPPV vs. Supplemental O₂ (controls)
- Re-intubation 72% vs. 69% (RR 1.04, CI 0.78-1.38)
- No differences in ICU or hospital LOS or mortality, which was 31% in both arms
- Potential drawback was sample size

Keenan et al, JAMA 2002;287:3238-44

NIV Does Not Reduce Reintubation in Post-extubation Respiratory Failure



Esteban et al, NEJM 2004;350:2452-60

NIV in Post-Extubation Respiratory Distress

- RCT of NIV vs. Conventional Therapy (well matched)
- Of 993 patients in 37 ICUs/8 countries, 221 had respiratory distress within 48 hrs of extubation and were randomized

Variable	Control n=107	NIV n=114	P
Reintubation	48%	48%	0.89
Time to reintubation	2.5 h	12 h	0.02
ICU length of stay	18 d	18 d	0.59
ICU mortality	14%	25%	0.05
Hospital mortality	25%	33%	0.11

High risk patients benefit from NIV to prevent extubation failure

- **Nava** studied 97 at risk patients (COPD, CHF, poor cough, abundant secretions)
- NIV group had less reintubation (8% vs 24%, $p=0.03$) and lower mortality (6% vs 18%, $p=0.01$)
- **Ferrer** studied 162 at risk patients (>65 , CHF, APACHE >12 on day of extubation)
- NIV group (19 hrs on I/E 14/5 cm H₂O) had less reintubation (16% vs 27%, $p=0.029$) and lower ICU mortality (3% vs 12%, $p=0.015$), no change in 90 day mortality
- **Girault** studied 208 patients in 13 ICUs and found that NIV reduced the risk of post-extubation respiratory failure
- Those with COPD and CHF benefited the most in these studies

Nava S, CCM 2005;33:2465-2470

Ferrer M, AJRCCM 2006;173:164-170

Girault C, AJRCCM 2011;184:672-79

NIV : Patient Selection is Key

Exclude those with contraindications:

- Respiratory arrest
- Medically unstable
- Unable to protect airway
- Excessive secretions
- Uncooperative or agitated
- Unable to fit mask
- Recent upper airway or GI surgery

Tracheostomy in Respiratory Failure

- 3 recent large RCTs of early tracheostomy
 1. 419 randomized: shorter time on vent **but** no effect on VAP, LOS, or mortality
 2. 216 randomized: no effect on MV time or LOS but less sedation, haloperidol, and better earlier mobility
 3. 909 randomized: no effect on mortality, ICU or hosp LOS, was associated with less sedation

1. Terragni P, JAMA 2010;303:1483-1489
2. Trouillet J, Ann Intern Med 2011;154:373-83
3. Young D, ISICEM 2009
4. Freeman and Morris, CCM 2012;40:2890-96

ONLINE FIRST

Effect of Pressure Support vs Unassisted Breathing Through a Tracheostomy Collar on Weaning Duration in Patients Requiring Prolonged Mechanical Ventilation

A Randomized Trial

Among LTAC patients, time to wean was shorter in those with trach collar treated with SBT type trials than those treated with PSV

Conclusions on Weaning

- Systematic approaches to weaning have been consistently supported by Grade A evidence
- Weaning protocols *intersect* with sedation protocols and should be considered in tandem and implemented in an interdisciplinary manner using tools (e.g., PDAs) to increase adherence
- SBTs should be done every day unless specifically contraindicated, and this can be driven by therapists, nurse, or computers
- In patients with COPD, NIV can be used as a bridge to earlier extubation
- NIV (in the absence of chronic lung disease) is not supported for weaning or for prevention of extubation failure



Estimated PaO₂/FiO₂

SpO₂

FiO₂

Age years

Ventilator

PEEP cms H₂O

Temp. °

Submit

Estimated value: **463.46**

Pandharipande PP et.al. Crit Care Med. 2009 Apr;37(4):1317-21

Rice TW et.al. Chest. 2007 Aug;132(2):410-7



Estimated PaO₂/FiO₂

SpO₂ FiO₂ Age yearsVentilator PEEP cms H₂OTemp. °

Estimated value: **214.99**

Estimated PaO₂/FiO₂

SpO₂
FiO₂
Age years
Ventilator
PEEP cms H₂O
Temp. °

Submit

Estimated value: **168.08**

Estimated PaO₂/FiO₂

SpO₂
FiO₂
Age years
Ventilator
PEEP cms H₂O
Temp. °

Estimated value: **91.992**



VANDERBILT UNIVERSITY
MEDICAL CENTER

Acute Brain Injury & SCCM Guidelines For Pain, Agitation, Delirium (PAD)



E. Wesley Ely, MD, MPH

Professor of Medicine

Vanderbilt University, Nashville, TN

VA TN Valley Health Care System GRECC



VANDERBILT UNIVERSITY
MEDICAL CENTER

Critical Illness Brain Injury (CIBI)



E. Wesley Ely, MD, MPH

Professor of Medicine

Vanderbilt University, Nashville, TN

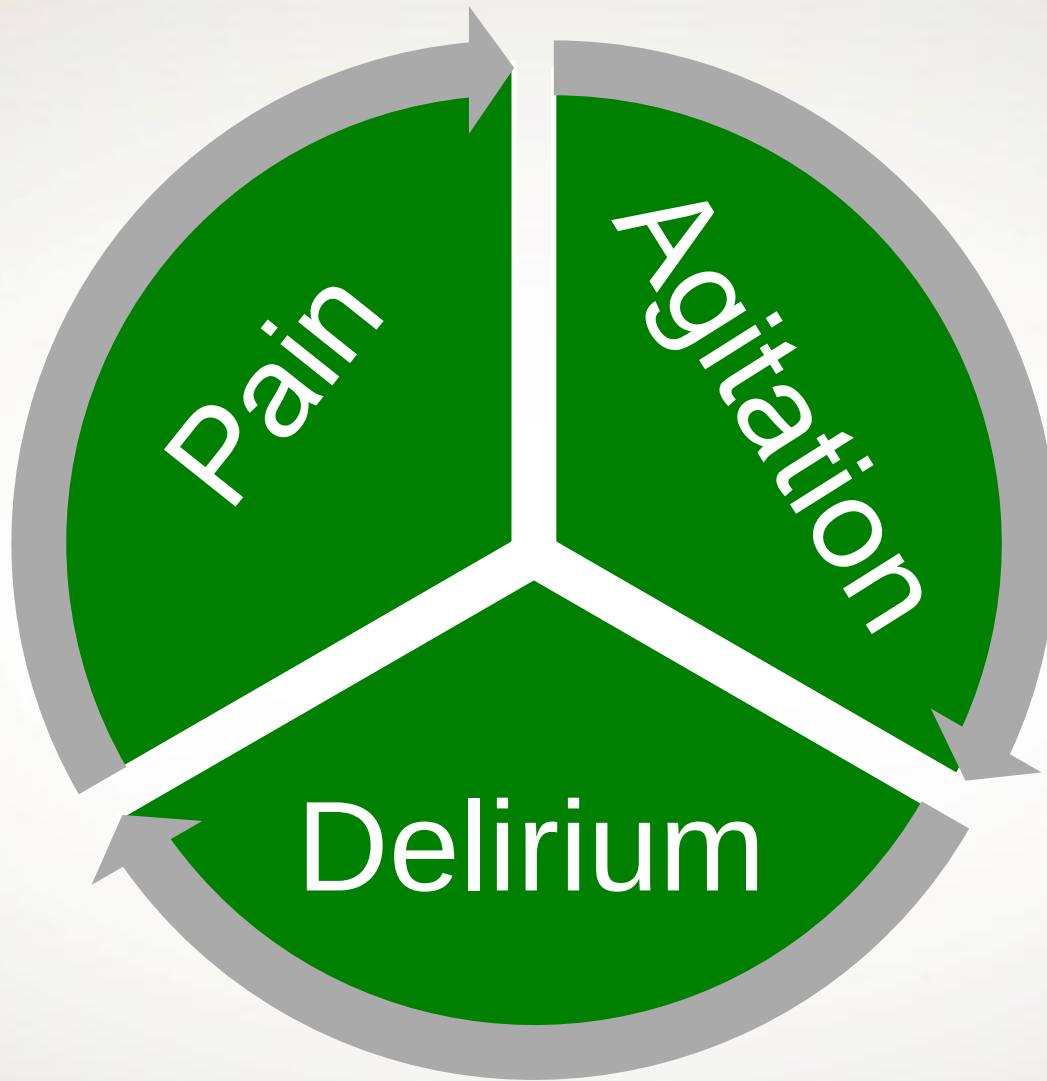
VA TN Valley Health Care System GRECC



Disclosures: ICU Physician Vanderbilt

- Abbott, Hospira, Orion
- NIH and VA U.S. Federal Funding
- Author of PAD Guidelines of SCCM 2013
- Chair of SCCM Delirium section for PAD
- Co-Chair of SCCM ICU Liberation project to aid world-wide implementation







Special Article

Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

Juliana Barr, MD, FCCM¹; Gilles L. Fraser, PharmD, FCCMP²; Kathleen Pantillo, RN, PhD, FAAN, FCCM³; E. Wesley Ely, MD, MPH, FACP, FCCM⁴; Céline Gélinas, RN, PhD⁵; Joseph F. Dasta, MSc, FCCM, FCCP⁶; Judy E. Davidson, DNP, RN⁷; John W. Devlin, PharmD, FCCM, FCCP⁸; John P. Kress, MD⁹; Aaron M. Joffe, DO¹⁰; Douglas B. Coursin, MD¹¹; Daniel L. Herr, MD, MS, FCCM¹²; Avery Tung, MD¹³; Bryce R. H. Robinson, MD, FACS¹⁴; Dorrie K. Fontaine, PhD, RN, FAAN¹⁵; Michael A. Ramsay, MD¹⁶; Richard R. Riker, MD, FCCM¹⁷; Curtis N. Sessler, MD, FCCP, FCCM¹⁸; Brenda Pun, MSN, RN, ACNP¹⁹; Yoanna Skrobik, MD, FRCP²⁰; Roman Jaeschke, MD²¹

New guidelines emphasize individual symptom management

**OLD
(2002)**

Clinical Practice Guidelines for the sustained use of sedatives and analgesics in the critically ill adult

Jacobi, CCM 2002

**New
(2013)**

Clinical Practice Guidelines for the management of Pain, Agitation, and Delirium in adult patients in the Intensive Care Unit

Barr, CCM 2013

icudelirium.org

RESEARCH DESIGNED TO TURN
MIRRORS INTO WINDOWS



HOME

DELIRIUM

SEDATION

OUTCOMES

REFERENCES

OUR GROUP

ICU DELIRIUM AND COGNITIVE IMPAIRMENT STUDY GROUP

delirium overview and how to diagnose it



Delirium is confusion that comes on very fast, sometimes in just a few hours. When someone becomes delirious, it means that they can not think clearly, have trouble paying attention and are not aware of what is going on around them. Sometimes they may even see or hear things that are not really there but seem very real to them.



Risk Factors
Study

Terminology and
Mnemonics

Assessment

Implementation
of CAM-ICU

FAQ

Patients and
Family



Video: Some common sedatives could negatively affect the brain



Video: Dr. Valerie Page - Delirium in ICU



Video: 10 Key Points Tutorial



Video: Using the CAM-ICU



Video: Improving the lives of people we will never meet

ABCDEs of Prevention and Safety

ABCDE is a standard bundle of ICU measures that include spontaneous Awakening and Breathing Coordination, attention to the Choice of Sedation, Delirium monitoring, and Early mobility and exercise. All individual components of this bundle are evidence based and can help standardize communication, improve interdisciplinary patient care, reduce mortality, and improve long-term cognitive and functional outcomes.

ABCDE Chest Article

ABCDE Crit Care Med Article

WALL STREET JOURNAL covers ABCDE

ABCDE Bedside Checklist

ABCDE Pocket Reference

ABCDE Education Slides

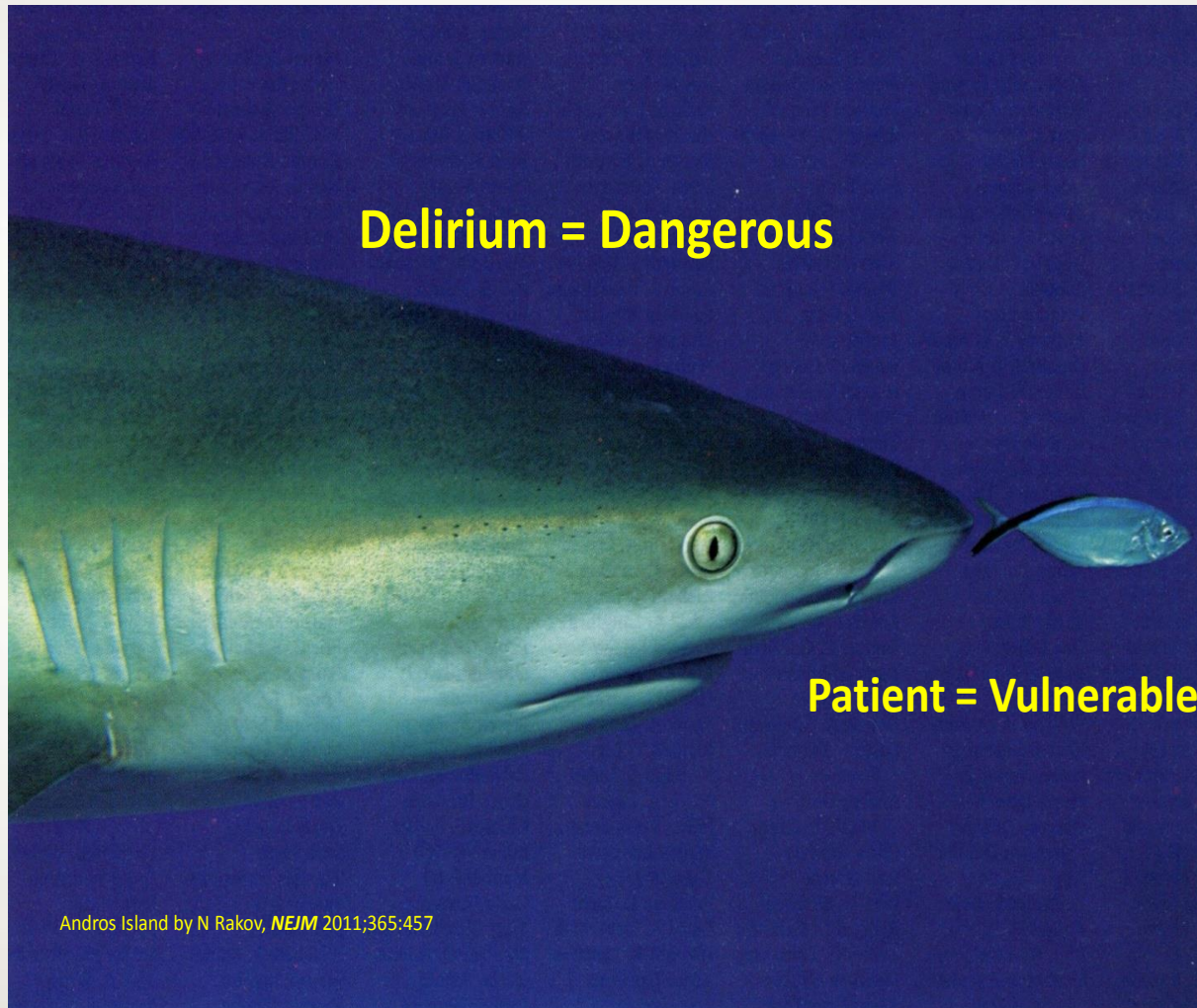
CAM-ICU Training Slides

assessment resources for ICU Delirium

sedation



Take Home Message



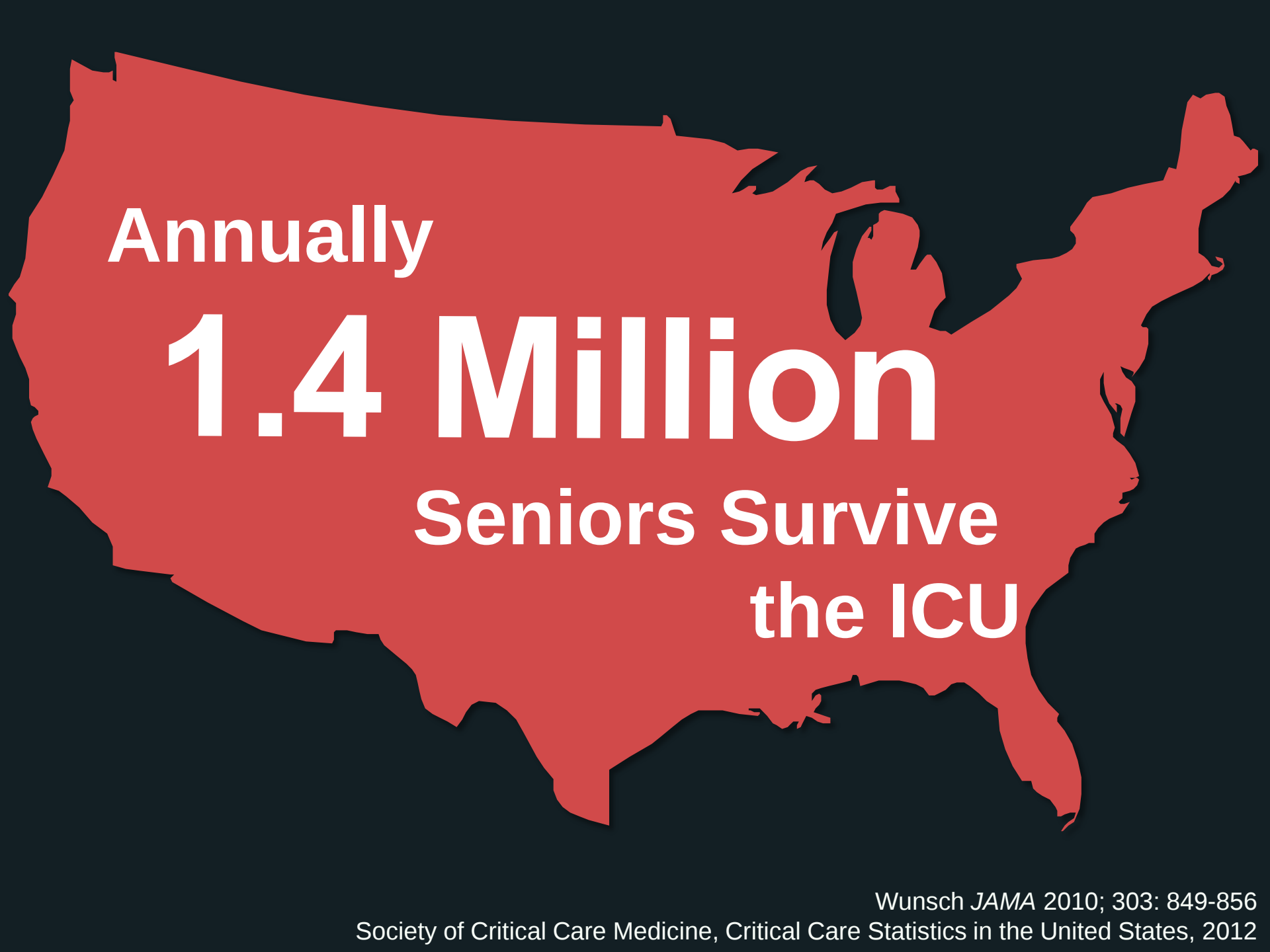
6 out of 10 ICU patients are ≥ 65



Angus *Crit Care Med* 2006; 34: 1016-1024

Angus *JAMA* 2000; 284: 2762-2770

Society of Critical Care Medicine, Critical Care Statistics in the United States, 2012



Annually

1.4 Million

**Seniors Survive
the ICU**

Wunsch *JAMA* 2010; 303: 849-856

Society of Critical Care Medicine, Critical Care Statistics in the United States, 2012

50-70%

Cognitively Impaired

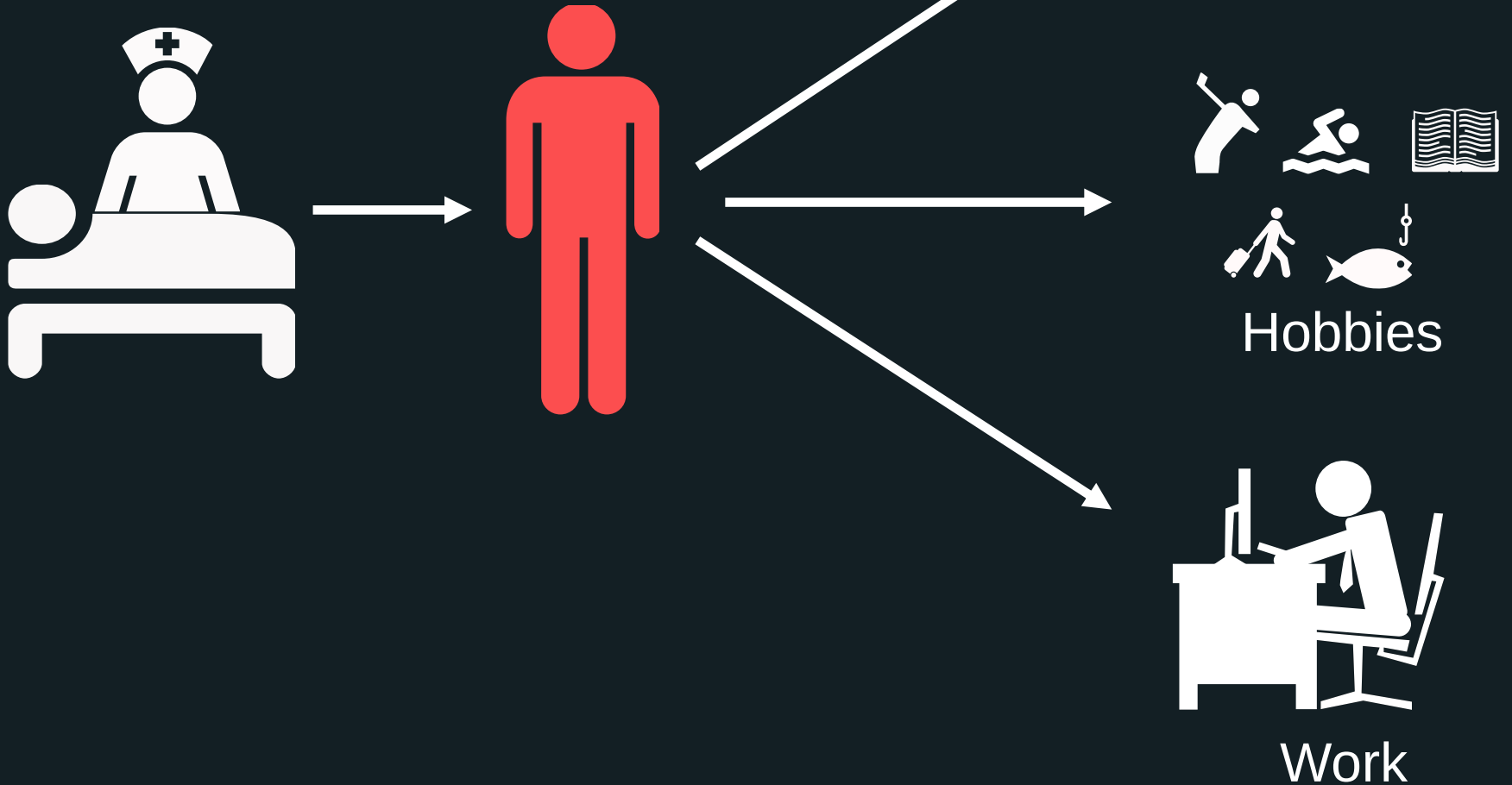
Wolters *Intensive Care Med* 2013; 39: 376
Jackson *AJRCCM* 2010; 182: 183
Girard *Crit Care Med* 2010; 38: 1513

60-80%

Functionally
Impaired



ICU Survivorship



“

...like it was in a huge, empty gray space, sort of like a monstrous underground parking garage with no cars, only me, floating or seeming to float, on something...

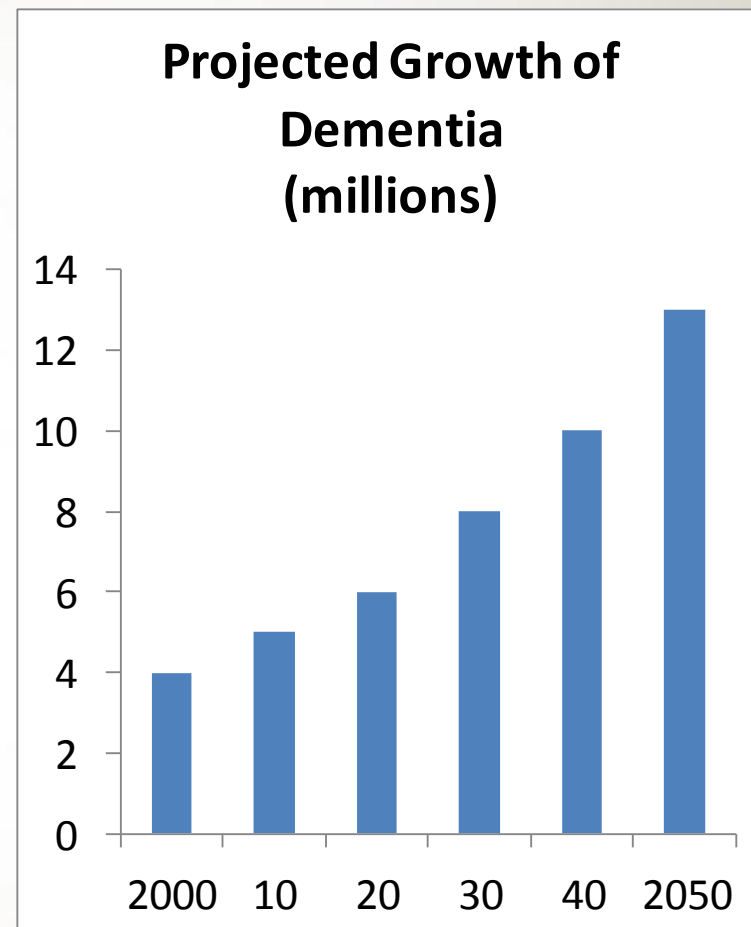
-SB



By Doug Kapustin for USA TODAY

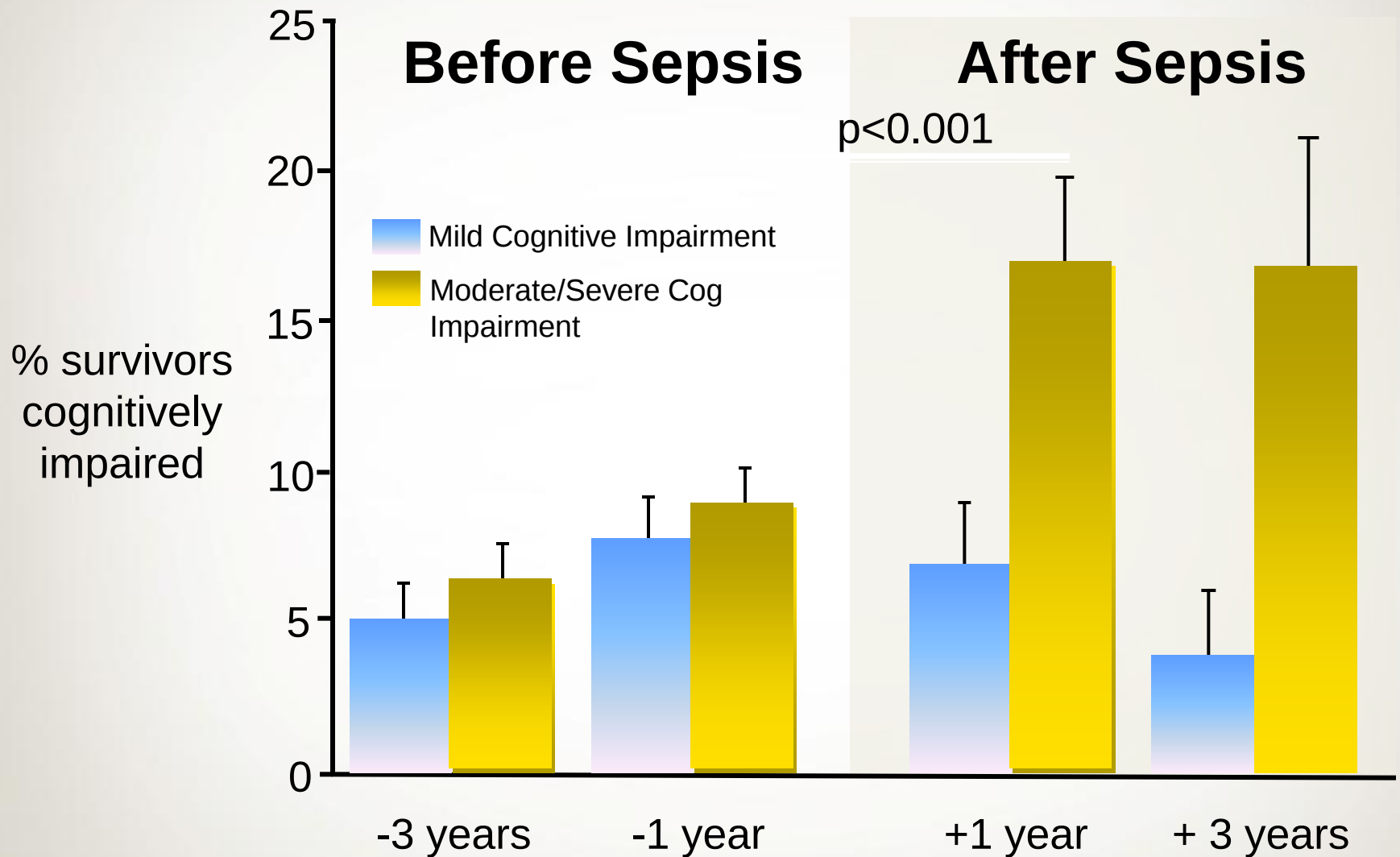
"No cure and no promise of a cure": Bob Blackwell was diagnosed with Alzheimer's in 2006 at age 64. His wife, Carol, says the disease is robbing him of his ability to communicate clearly.

We must 'find a cure' to save memories



Time in Decades

Cognitive Impairment: Sepsis



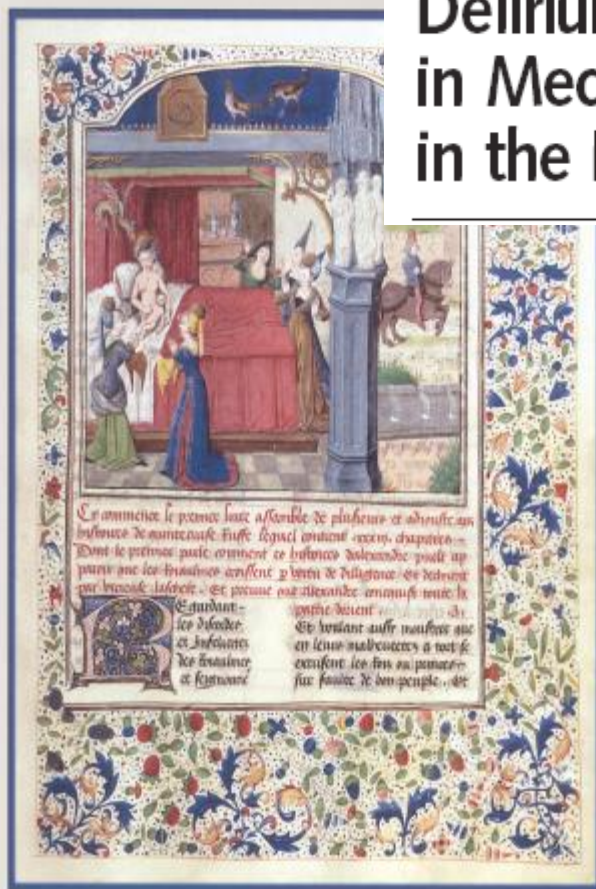
JAMA[®]

The Journal of the American Medical Association

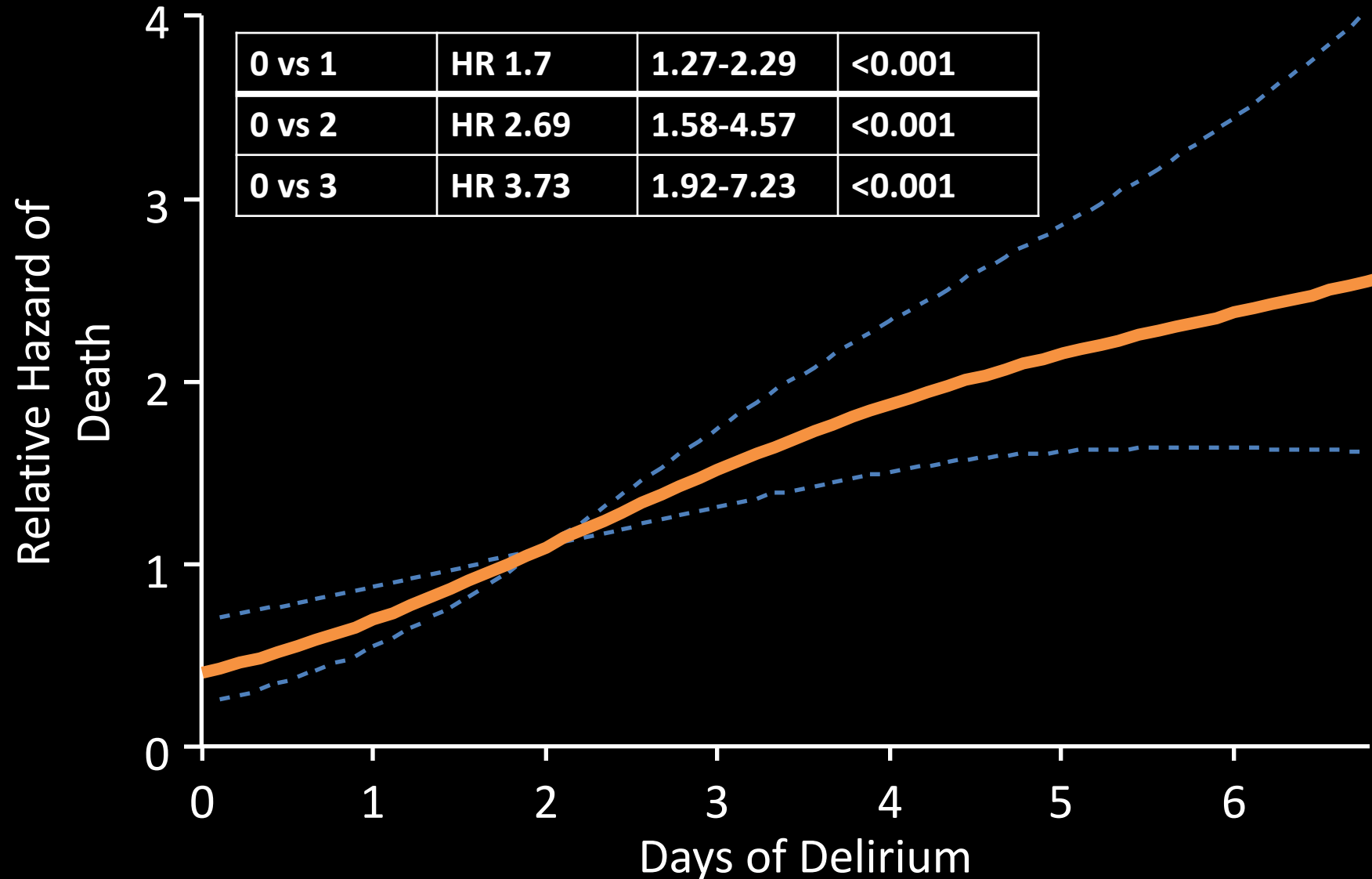
CARING FOR THE
CRITICALLY ILL PATIENT

Ely EW, JAMA 2004;291:1753-62

Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit

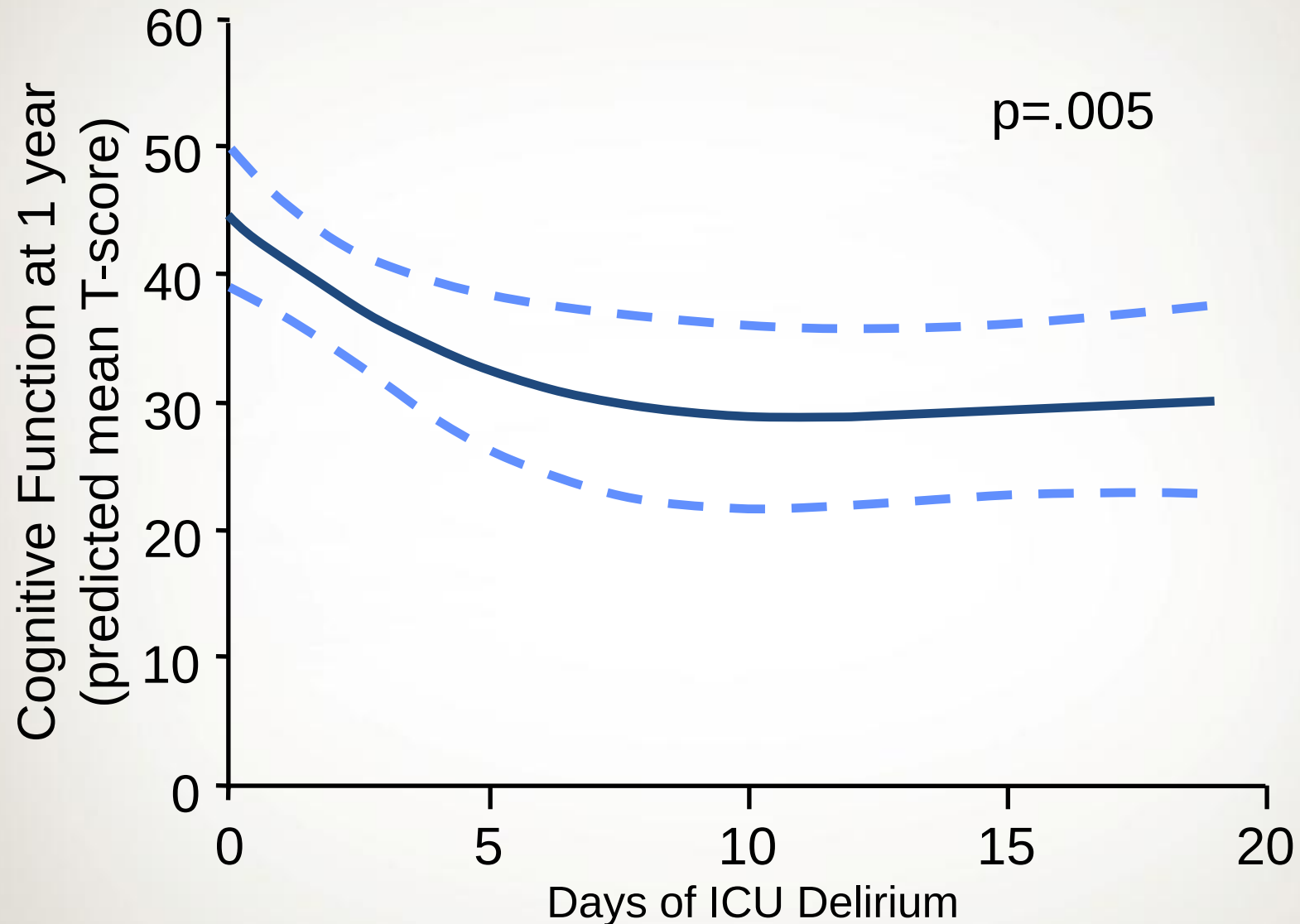


Delirium Duration & Mortality



Shehabi Y, et al. CCM 2010; 38:2311–2318

Delirium and Long-Term Cognitive Outcomes

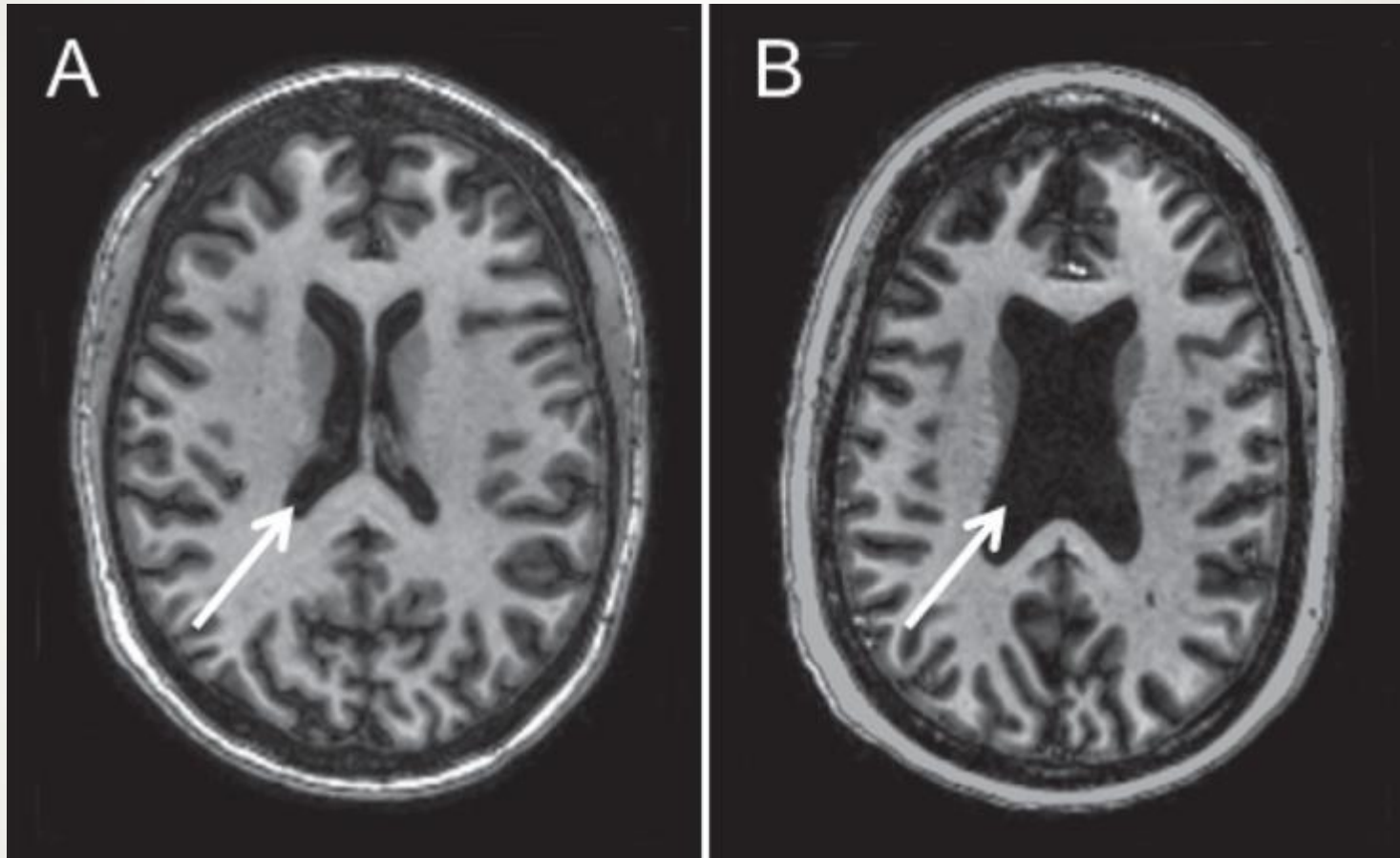


Bringing to light Risk factors And Incidence of Neuropsychological dysfunction in ICU survivors



BRAIN ICU

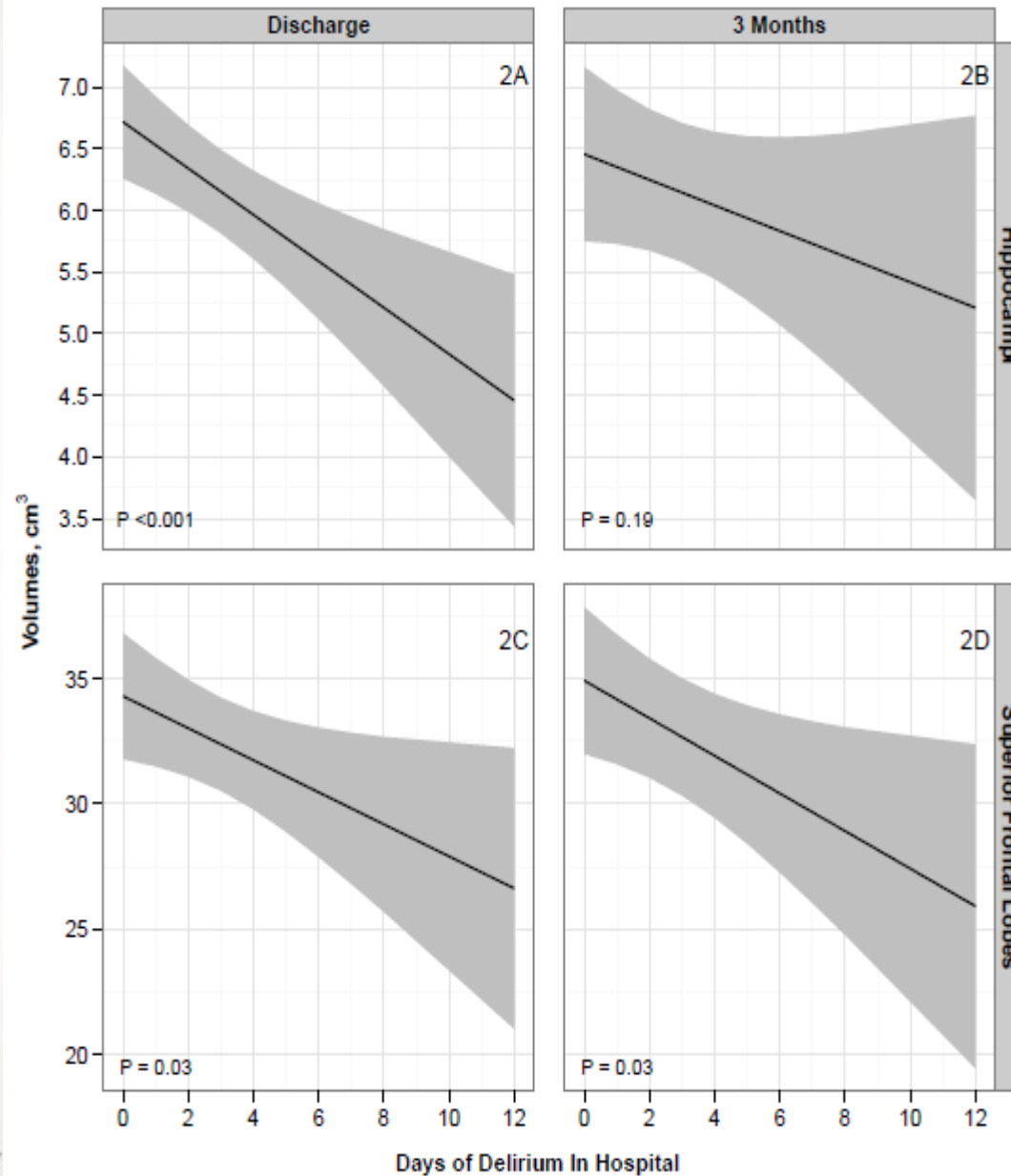
Delirium and Brain Atrophy



(A) 46 year old, no delirium

(B) 42 year old, 12 days of delirium

The VISIONS MRI Studies



Gunther M et al. CCM
2012;40:2022-32

Persistent cognitive impairment, hippocampal atrophy and EEG changes in sepsis survivors

Alexander Semmler,^{1,6} Catherine Nichols Widmann,¹ Thorsten Okulla,¹ Horst Urbach,² Markus Kaiser,^{3,7} Guido Widman,⁴ Florian Mormann,^{4,8} Julia Weide,¹ Klaus Fliessbach,⁴ Andreas Hoeft,³ Frank Jessen,⁵ Christian Putensen,³ Michael T Heneka¹

- Bonn Germany, 2 center 6-24 month follow-up of 25 septic and 19 non-septic ICU survivors
- Sepsis survivors showed cognitive deficits in verbal learning and memory
- Significant reductions of hippocampal volume vs. controls
- More low frequency EEG activity indicating brain dysfunction

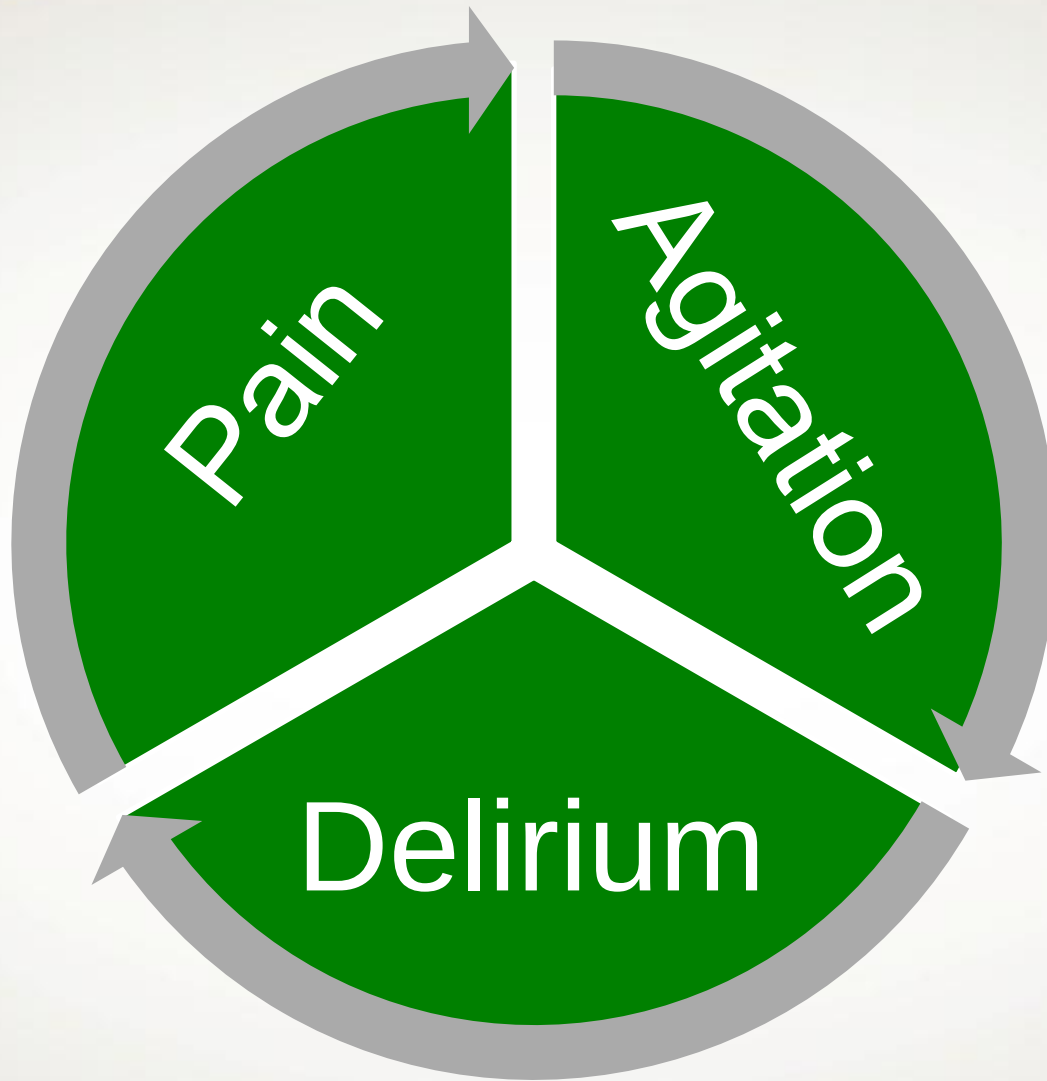
THE LANCET

Volume 372 · Number 9634 · Pages 177–262 · July 19–25, 2008

www.thelancet.com

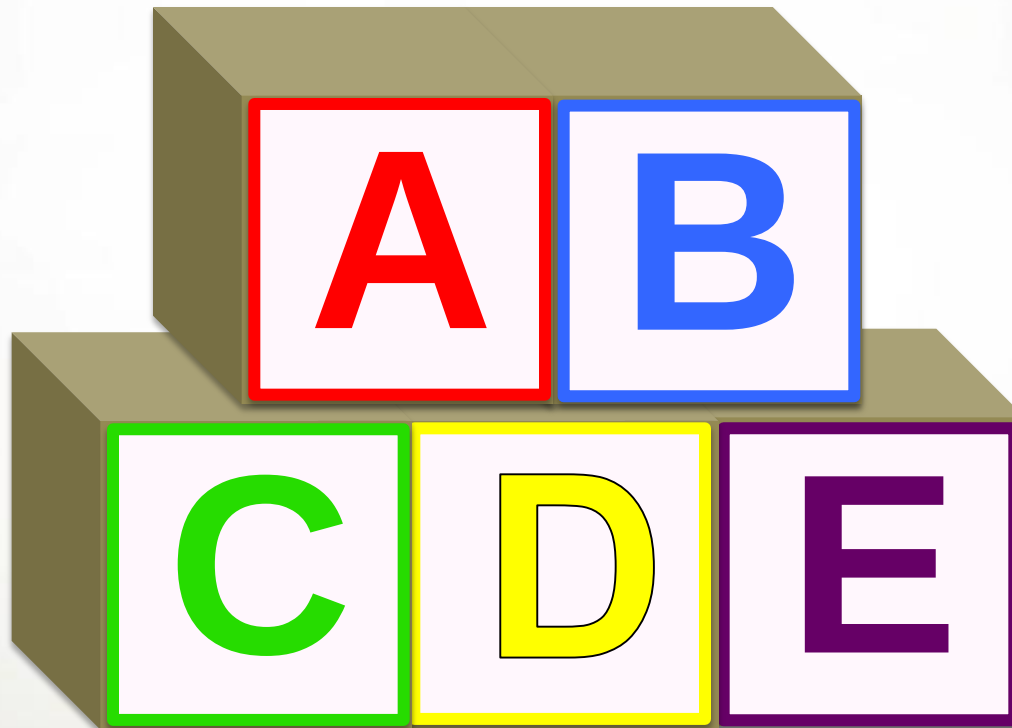
"Dementia is perhaps the cruellest manifestation of ageing, inexorably melting away all that which makes us individual and human."

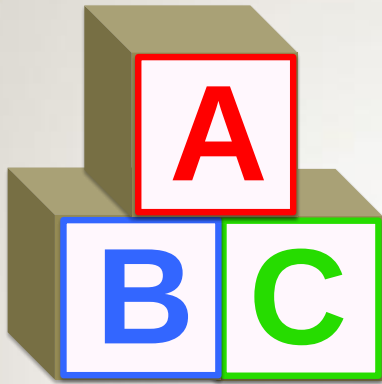
See Editorial page 177



ABCDEs:

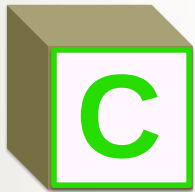
*Building blocks of managing
Pain, Agitation & Delirium*





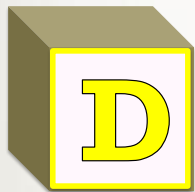
Awake and Breathing Coordination

- ↓ Duration of mechanical ventilation
- ↓ Duration of coma
- ↓ Mortality



Choose light sedation & avoid benzos

- ↓ Duration of mechanical ventilation
- ↓ Mortality
- ↓ Delirium



Delirium monitoring & management

- ↑ Delirium detection

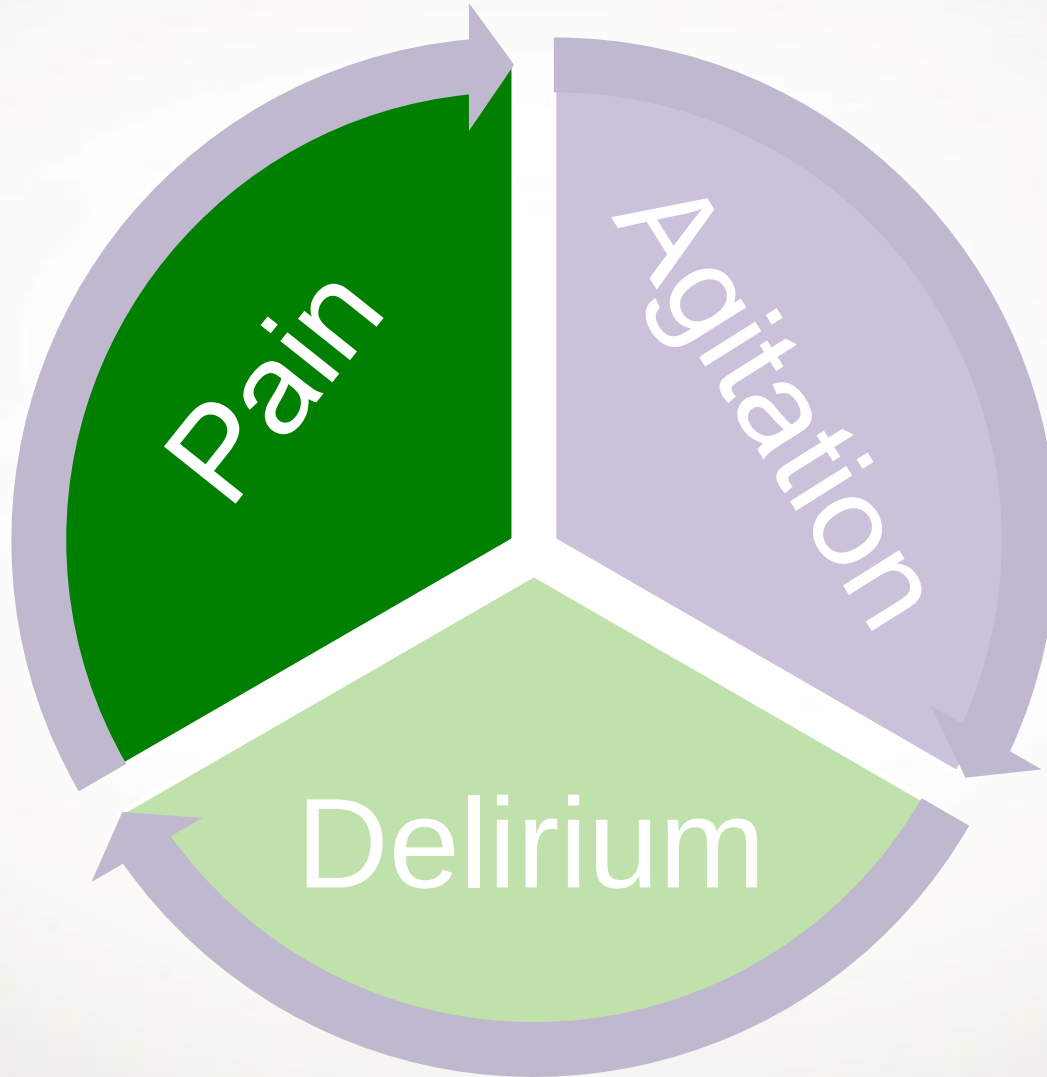


Early Mobility & Environment

- ↓ Duration of delirium
- ↓ Disability
- ↓ ICU Length of Stay
- ↓ Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Vasilevskis et al Chest 2010;138:1224-1233
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 1012;78:1026-33

Pain, Agitation, and Delirium Are Interrelated



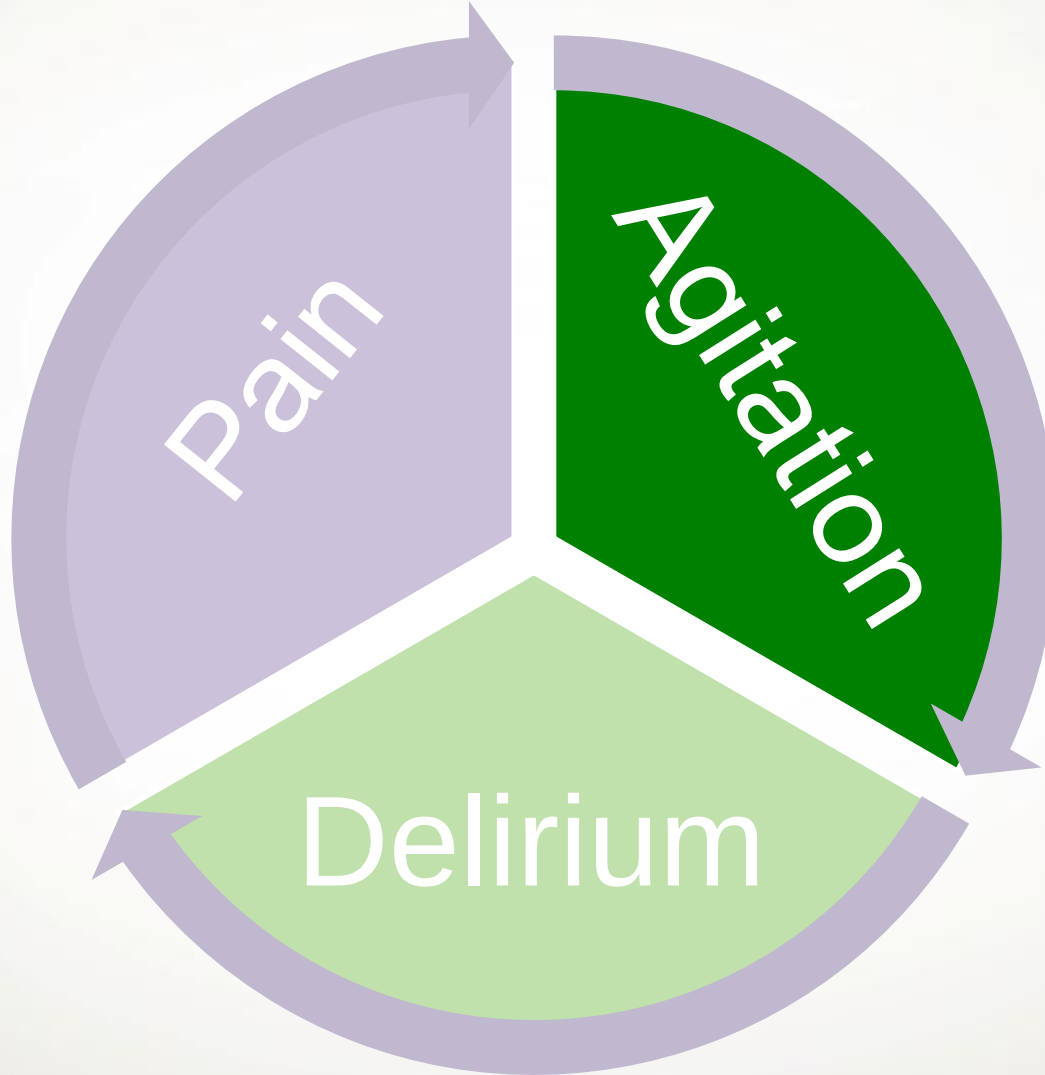
2013 PAD Guidelines:

“Pain should be routinely monitored
in all adult ICU patients”

Grade 1B Recommendation

Crit Care Med. 2013;41:263-308

Pain, Agitation, and Delirium Are Interrelated



Targeted Level of Consciousness



Choose Target RASS

Assess Actual RASS

**Modify treatment so
Actual = Target**

Patient-Centered Care:

Targeting, Protocolizing, and Modifying the Environment

2013 PAD Guidelines:

“We recommend either daily sedation interruption or a light level of target sedation be routinely used...”

Grade 1B Recommendation

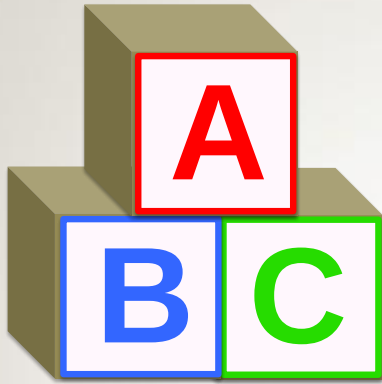
Crit Care Med. 2013;41:263-308

2013 PAD Guidelines:

“We recommend that sedative medications be titrated to maintain a light* rather than deep level of sedation”

Grade 1B Recommendation

**Light sedation = RASS 0 to -2*



Awake and Breathing Coordination

- ↓ Duration of mechanical ventilation
- ↓ Duration of coma
- ↓ Mortality



Choose light sedation & avoid benzos

- ↓ Duration of mechanical ventilation
- ↓ Mortality
- ↓ Delirium



Delirium monitoring & management

- ↑ Delirium detection



Early Mobility & Environment

- ↓ Duration of delirium
- ↓ Disability
- ↓ ICU Length of Stay
- ↓ Rehospitalization/Mortality

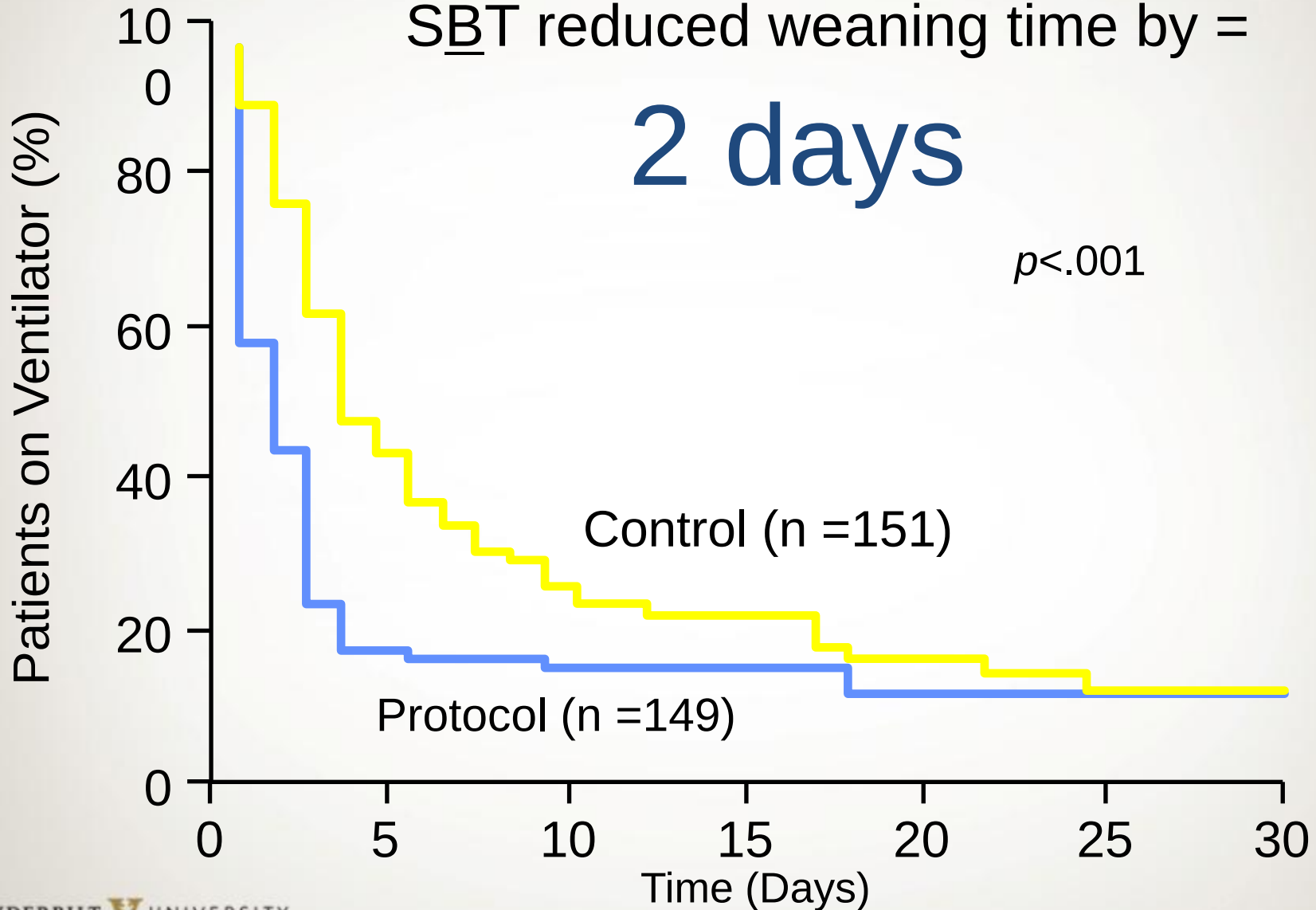
Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Vasilevskis et al Chest 2010;138:1224-1233
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 1012;78:1026-33

Liberating from Ventilator

SBT reduced weaning time by =

2 days

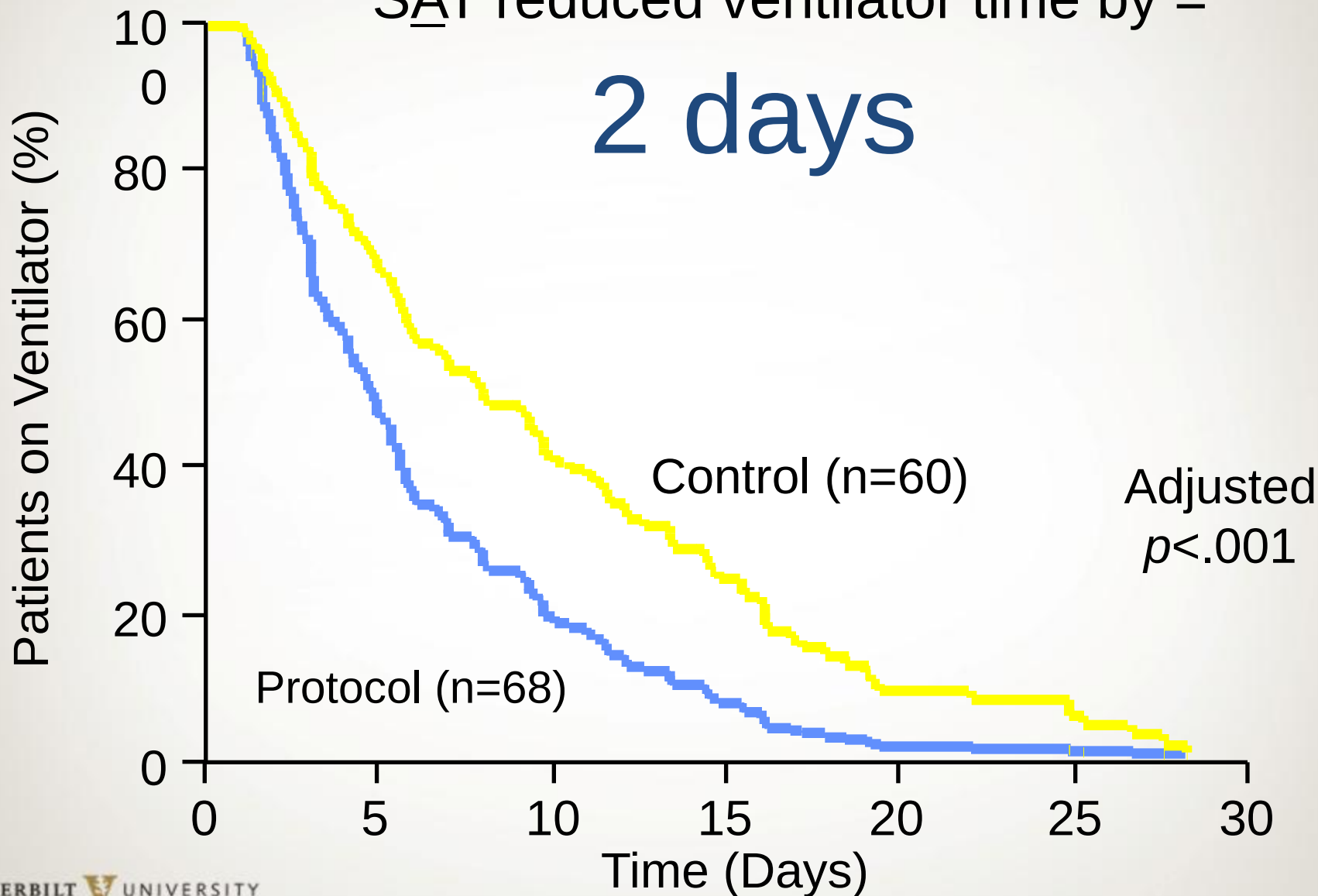
$p < .001$



Liberating from Sedation

SAT reduced ventilator time by =

2 days



SATs (Daily Interruption) Used in Minority Around World

- Canada – 40% get SATs (273 physicians in 2005)
- U.S. – 40% get SATs (2004-05)
- France – 10% get SATs (44 ICUs in 2005)
- Germany – 34% get SATs (214 ICUs in 2006)
- Brazil – 32% get SATs (1,015 MDs in 2008)
- UK – 28% get SATs, 82% use midazolam (2009)
- Belgium – 18% get SATs (587 nurses / 99 hospitals in 2012)

Mehta S, CCM 2006;34:374-80.

Tanios M, Proc Am Thorac Soc 2:A793, 2005

Devlin J, CCM 2006;34:556-57.

Payen JF, Anesthes 2007;106:687-95

Martin J and Spies C, Crit Care 2007;11:R124

Ramaswamy S, Intens Care Med (ESICM 2009)

Salluh J, Brazil, J Crit Care 2009

Sneyers B, Brussels, Abst #324 2012

THE LANCET

Volume 371 · Number 9607 · Pages 89–126 · January 12–18, 2008

www.thelancet.com

Articles

SAT + SBT = 4 day shorter ICU/hosp LOS

Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

Lancet 2008; 371: 126–34

See [Comment](#) page 95

Timothy D Girard, John P Kress, Barry D Fuchs, Jason WW Thomason, William D Schweickert, Brenda T Pun, Darren B Taichman, Jan G Dunn, Anne S Pohlman, Paul A Kinniry, James C Jackson, Angelo E Canonico, Richard W Light, Ayumi K Shintani, Jennifer L Thompson, Sharon M Gordon, Jesse B Hall, Robert S Dittus, Gordon R Bernard, E Wesley Ely

Articles

Statins for diabetic patients: meta-analysis
See page 117

Articles

Protocols for mechanically ventilated patients in intensive care
See page 126

Articles

Clinical signs predictive of severe illness in babies aged less than 2 months
See page 135

Seminar

Acute pancreatitis
See page 143

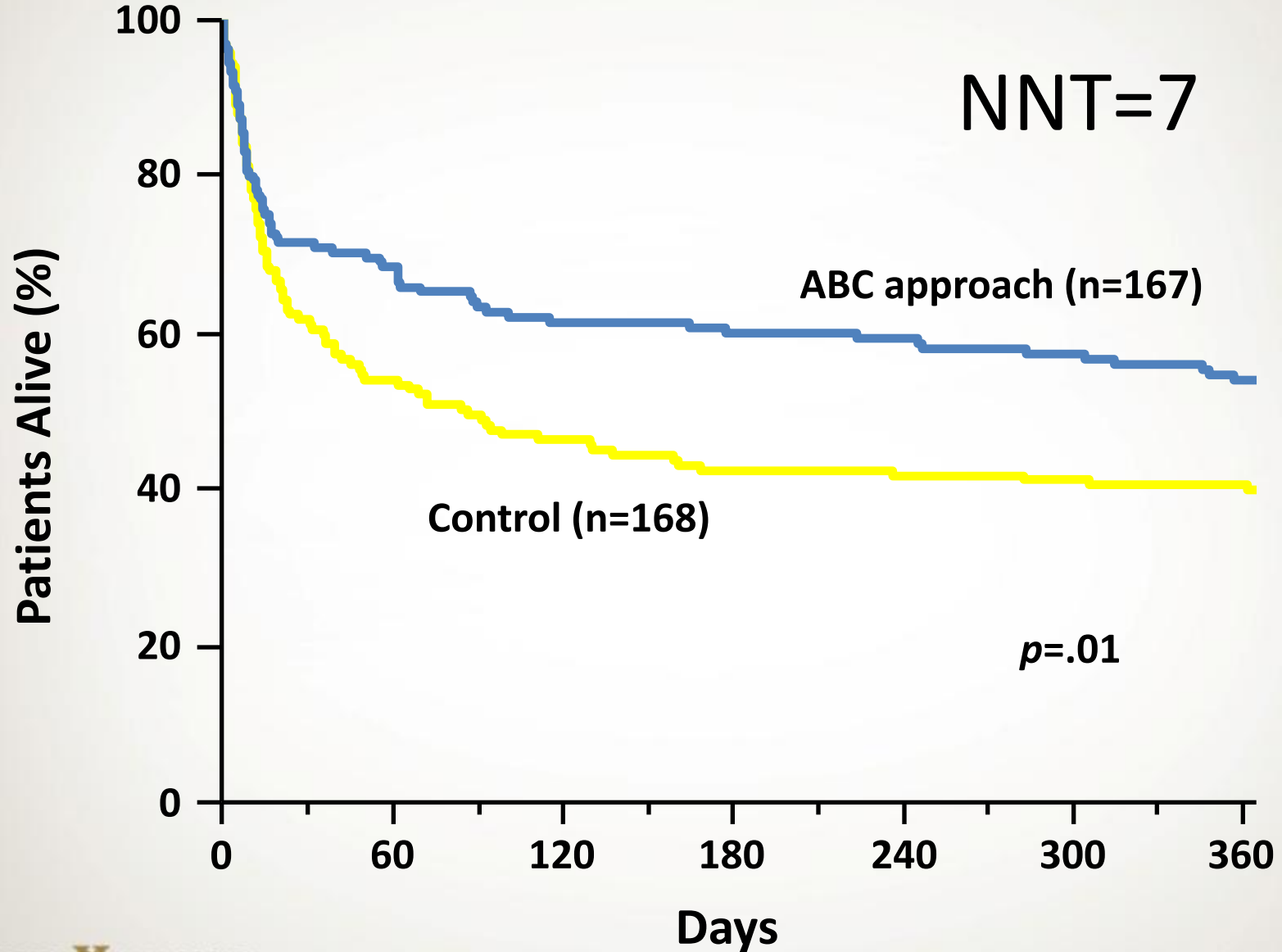
Series

Pregnancy 2: Interventions to reduce morbidity and mortality
See page 154

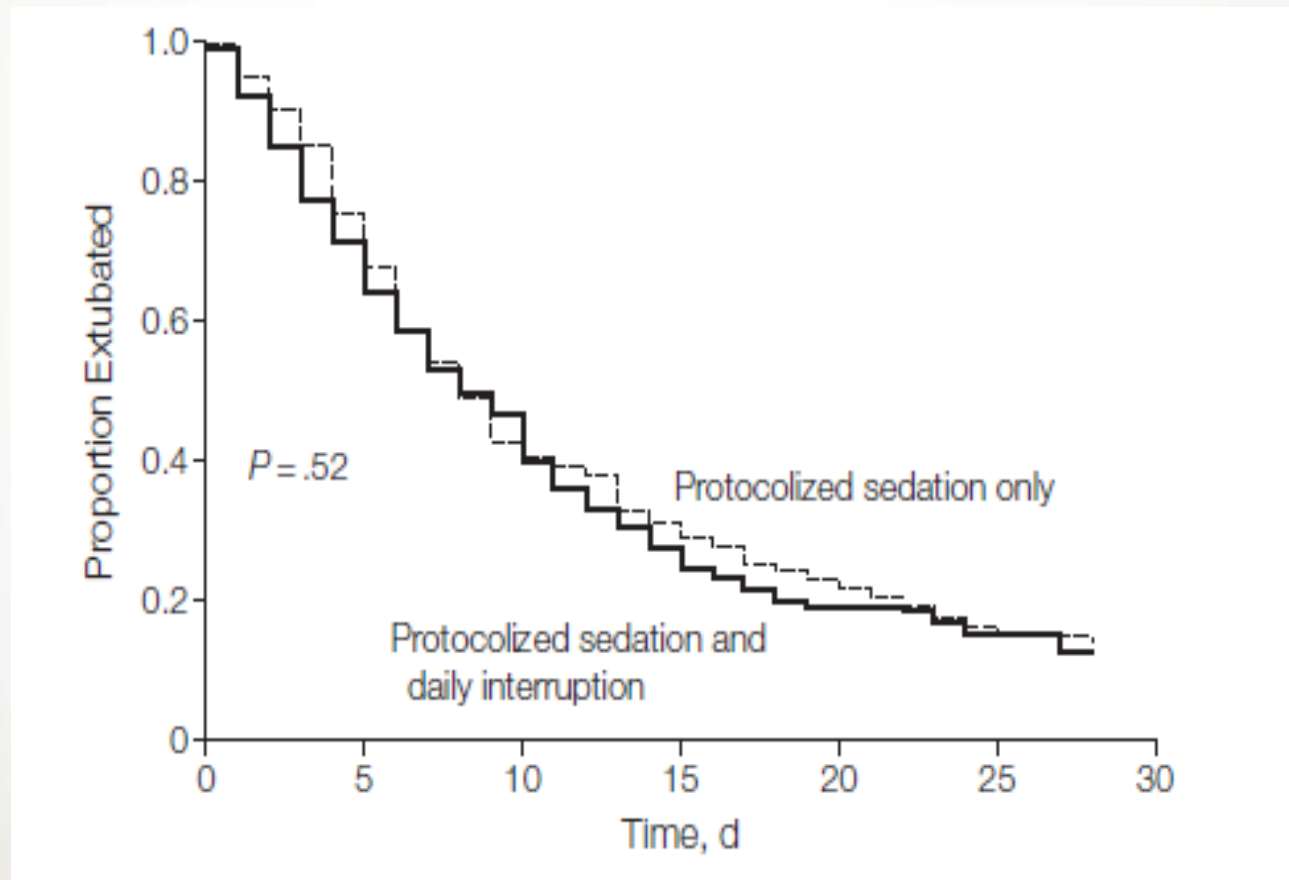
The Lancet (ISSN 0950-2688) is published weekly, except for the last issue in December which is a double issue. © 2008 Elsevier Ltd. All rights reserved. Elsevier Ltd's North American agent is Elsevier Inc., 360 Park Avenue South, New York, NY 10010-2100, USA. Tel: 212 633 3000. Fax: 212 633 3811. Periodical postage paid at New York NY and additional mailing offices. # 545-880 USPS CDSN P540095121
POSTMASTER: Send address changes to The Lancet, Elsevier Subscription Customer Service, 627 Sea Harbor Drive, Orlando, FL 32827-4000, USA.
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ABC Trial: One-Year Survival

NNT=7



Sedation Interruption in SLEAP



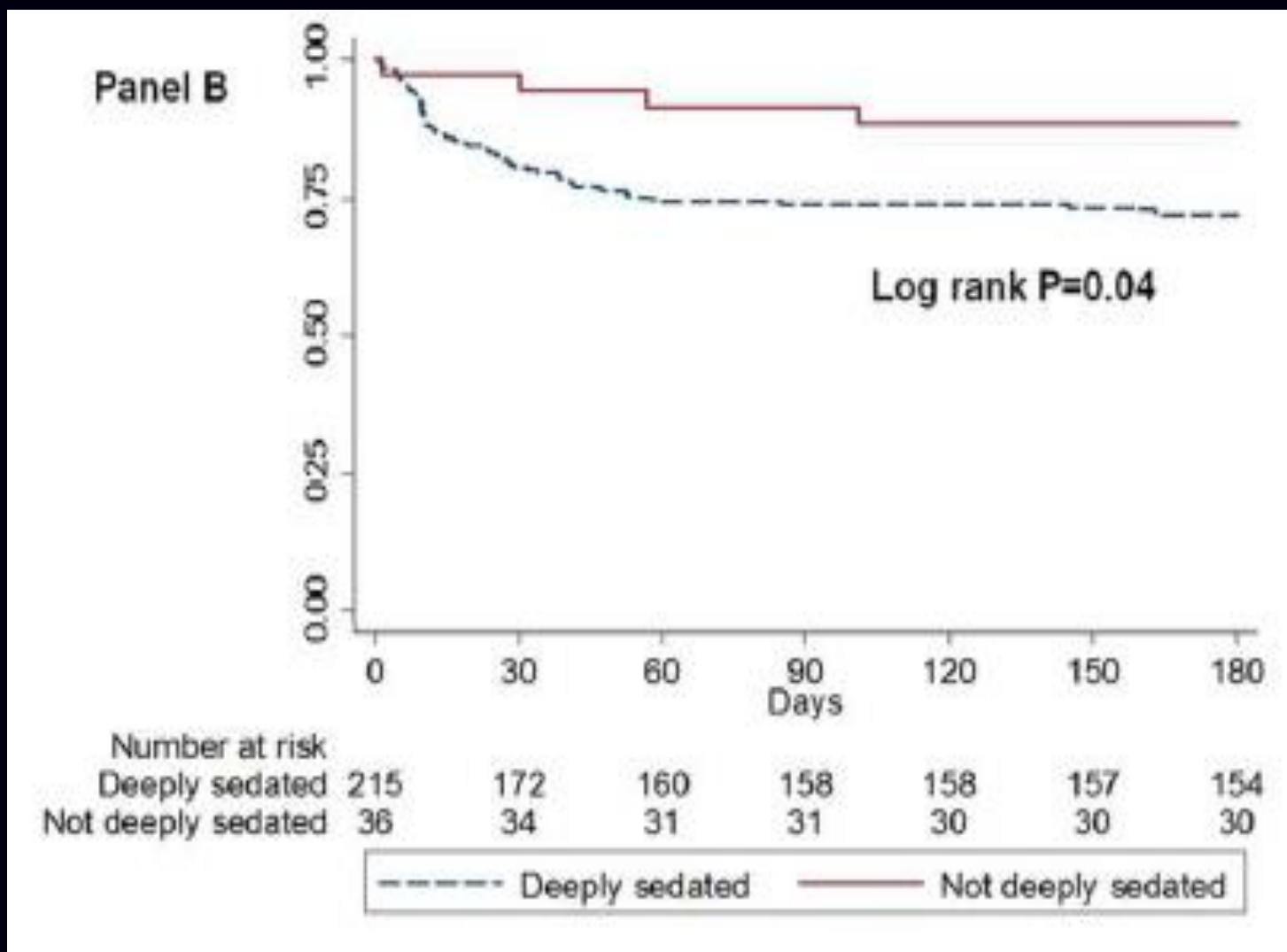
Benzodiazepine Use in Trials *

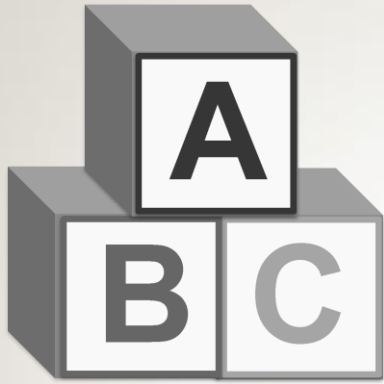
Study	Control	Treatment
Kress NEJM 2000	90 mg/day	53 mg/day
Girard ABC Lancet 2007	84 mg/day	54 mg/day
Mehta SLEAP JAMA 2012	82 mg/day	102 mg/day
OSCILLATE NEJM 2013	141 mg/day	199 mg/day

* All values converted and expressed as mean midazolam dose per patient, median for ABC study were 8 mg and 5 mg, respectively

SPICE Study – first 48 hours

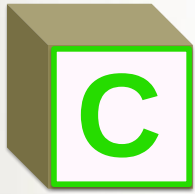
mean 50 mg/d benzos





Awake and Breathing Coordination

- ↓ Duration of mechanical ventilation
- ↓ Duration of coma
- ↓ Mortality



Choose light sedation & avoid benzos

- ↓ Duration of mechanical ventilation
- ↓ Mortality
- ↓ Delirium



Delirium monitoring & management

- ↑ Delirium detection



Early Mobility & Environment

- ↓ Duration of delirium
- ↓ Disability
- ↓ ICU Length of Stay
- ↓ Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Vasilevskis et al Chest 2010;138:1224-1233
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 1012;78:1026-33



A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial



Thomas Strøm, Torben Martinussen, Palle Toft

Summary

Background Standard treatment of critically ill patients undergoing mechanical ventilation is continuous sedation. Daily interruption of sedation has a beneficial effect, and in the general intensive care unit of Odense University Hospital, Denmark, standard practice is a protocol of no sedation. We aimed to establish whether duration of mechanical ventilation could be reduced with a protocol of no sedation versus daily interruption of sedation.

Methods Of 438 patients assessed for eligibility, we enrolled 140 critically ill adult patients who were randomised to

Lancet 2010; 375: 475–80

Published Online

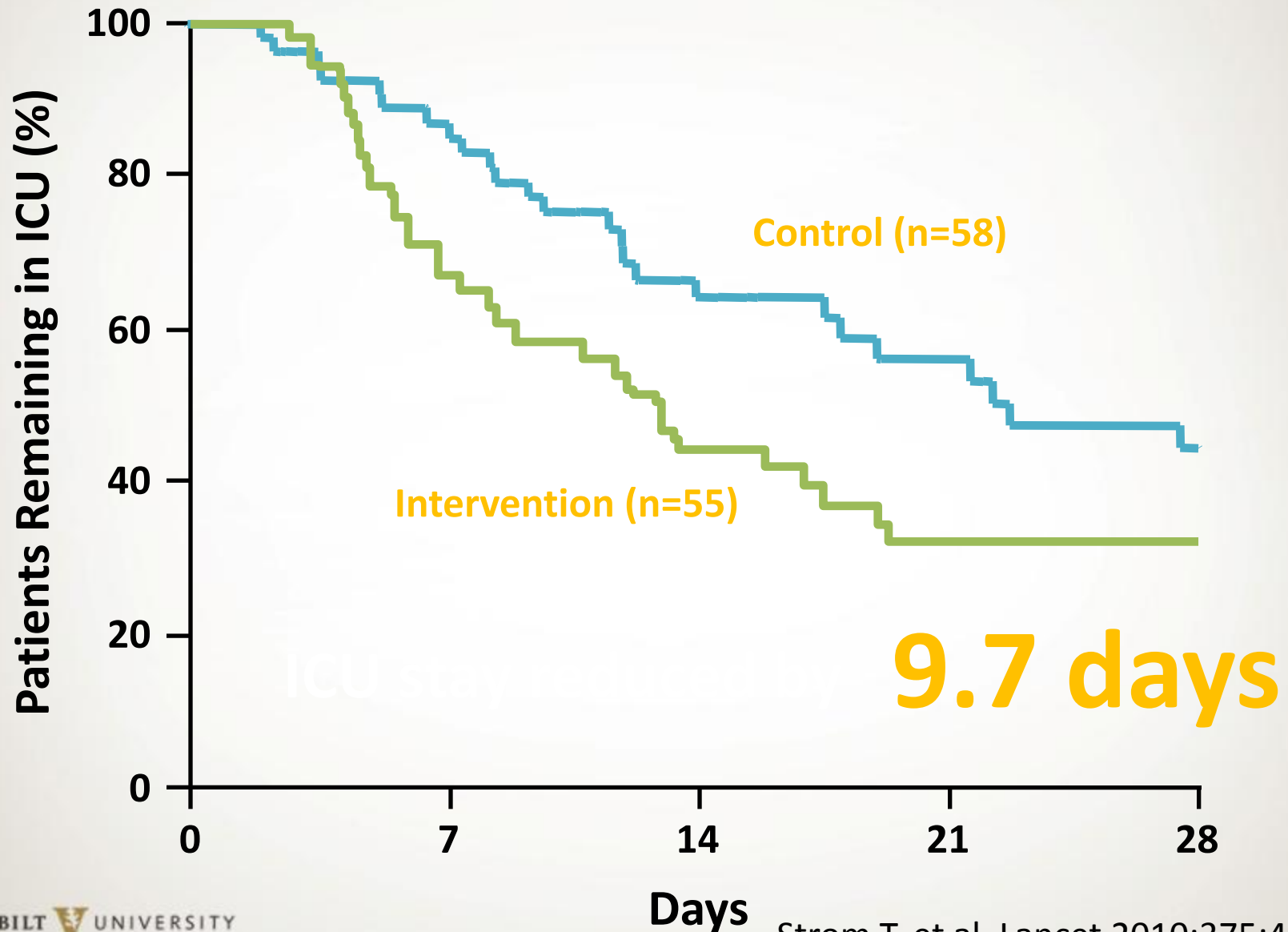
January 29, 2010

DOI:10.1016/S0140-

6736(09)62072-9

See [Comment](#) page 436

No Sedation: ICU Length of Stay



2013 PAD Guidelines: risk factors for ICU delirium

- Baseline
 - Pre-existing dementia
 - History of HTN or Alcoholism
 - High severity illness at ICU admission
- Duration of Coma (comment on new data)
- Medications
 - Narcotics – conflicting data
 - Benzodiazepines – identified as risk factor
 - Propofol – insufficient data
 - Dexmedetomidine – lower prevalence vs. benzodiazepines

2013 PAD Guidelines:

“We suggest that sedation strategies using non-benzodiazepines (propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines (midazolam or lorazepam)”

Grade 2B Recommendation

Crit Care Med. 2013;41:263-308

2013 PAD Guidelines: Benzodiazepines

1. General Choice: non-benzodiazepine sedation strategies preferred (propofol or dex), with statistically shorter ICU LOS (~0.5 day, $p=0.04$)
2. Benzodiazepines risk factor for delirium
3. Ventilated patients at risk for delirium prefer dexmedetomidine to benzodiazepine
4. Delirious ICU patients (excluding DTs and benzo w/drawal) - give dexmedetomidine (alpha-2) and not benzo (GABA)

Benzos vs. Propofol

Trials with better outcomes with propofol

Study/Year	Population	Outcome Improved
Grounds/1987	Cardiac Surgery	Faster Awakening
Aikenhead/ 1989	General ICU	More consistent awakening, faster weaning
McMurray, 1990	Cardiac Surgery	Faster Awakening
Carrasco, 1993	General ICU	More accurate sedation, faster awakening, lower costs
Roekaerts, 1993	Cardiac Surgery	Faster awakening, earlier extubation
Ronan, 1995	Surgical ICU	Faster awakening
Sherry, 1996	Cardiac Surgery	Lower costs
Chamorro, 1996	General ICU	Better vent synchrony, faster awakening
Barrientos-Vega, 1997	General ICU	Earlier Extubation
Weinbroum, 1997	General ICU	Faster Awakening
Sanchez-Izquierdo-Riera, 1998	Trauma ICU	Faster Awakening
McCollam, 1999	Trauma ICU	Less Oversedation
Hall, 2001	Mixed ICU	More accurate sedation, earlier extubation
Carson, 2006	Medical ICU	Fewer ventilator days

Called by lab to see patient's blood –
had been on propofol for 2 days



Propofol Infusion Syndrome

- Cardiac failure, rhabdomyolysis, severe metabolic acidosis, and renal failure
- Catecholamines and corticosteroids act as triggering factors
- Propofol impairs free fatty acid utilization and mitochondrial activity, leading to an imbalance between energy demand and utilization
- Avoid prolonged (>48 h) propofol sedation at doses higher than 5 mg/kg per h (>75 µg/kg/min)

Parke TJ, BMJ 1992;302:613–616

Hanna JP, Neurology 1998; 50:301–03

Perrier ND, CCM 2000;28:3071–3074

Cremer OL, Lancet, 2001;357:117–118

Benzos vs. Propofol

Trials finding no differences

Study/Year	Population	Outcome Improved
Searle/1997	Cardiac Surgery	None
Kress/2000	Medical ICU	None
Huey-Ling/2008	Cardiac Surgery	None

Benzos vs. Propofol

Trials finding better outcomes with benzodiazepines

Study/Year	Population	Outcome Improved
------------	------------	------------------

None

Benzos vs. Dexmedetomidine

Trials with better outcomes with dexmedetomidine

Study/Year	Population	Outcome Improved
Pandharipande/2007	Mixed ICU	More accurate sedation, more delirium/coma free days
Riker/2009	Mixed ICU	Lower prevalence of delirium, earlier extubation
Ruokonen/2009	Mixed ICU	Shorter duration of mechanical ventilation
Maldonado/2009	Cardiac Surgery	Lower incidence and duration of delirium
Esmaoglu/2009	Eclampsia	Shorter ICU LOS
Dasta/2010	Mixed ICU	Lower ICU costs
Jakob/2012	General ICU	Lighter sedation, fewer ventilator days

Benzos vs. Dexmedetomidine

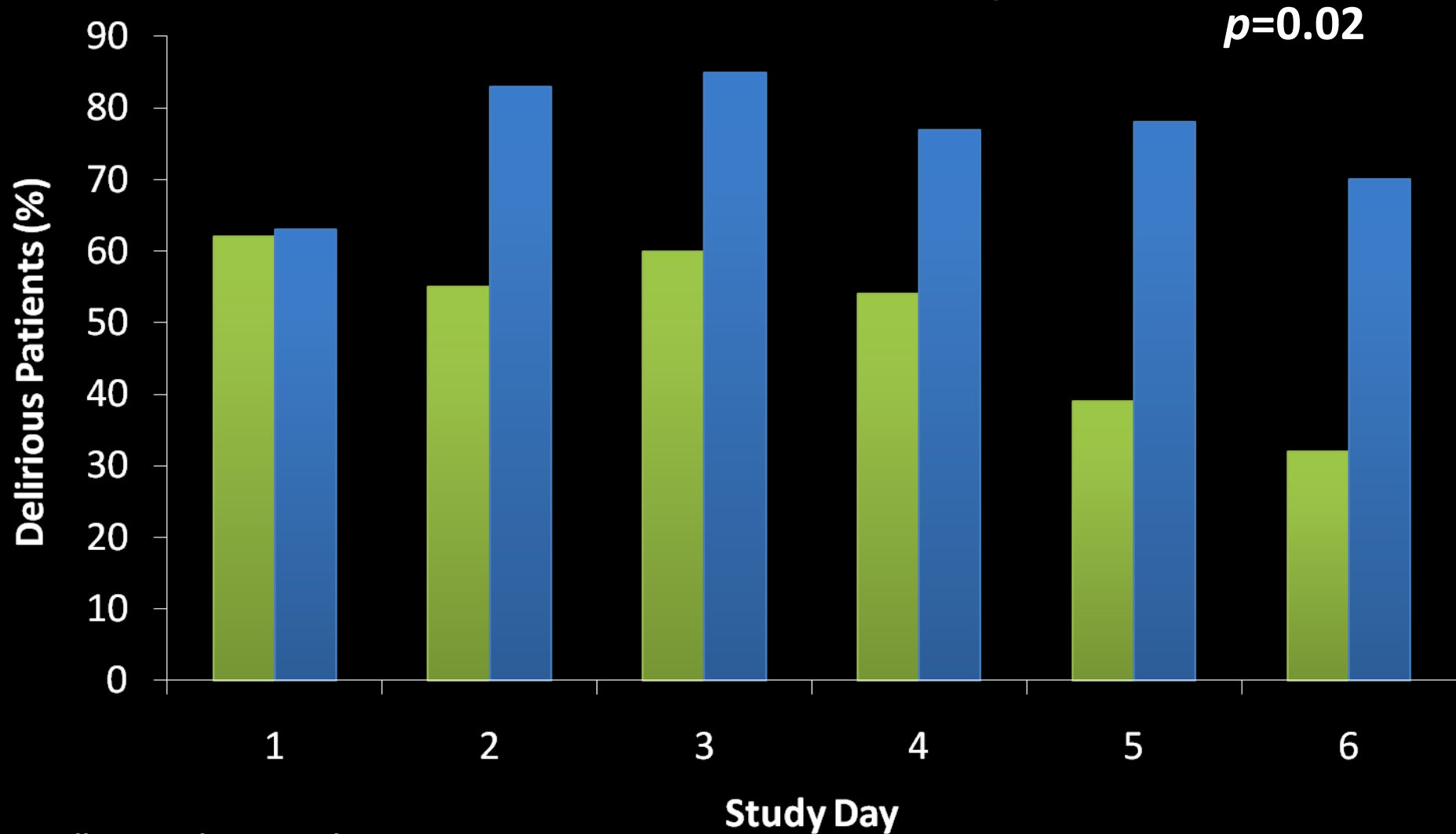
Trials with no difference in outcomes or better outcomes with benzodiazepines

Study/Year	Population	Outcome Improved
------------	------------	------------------

None

Daily Risk of Delirium in MENDS

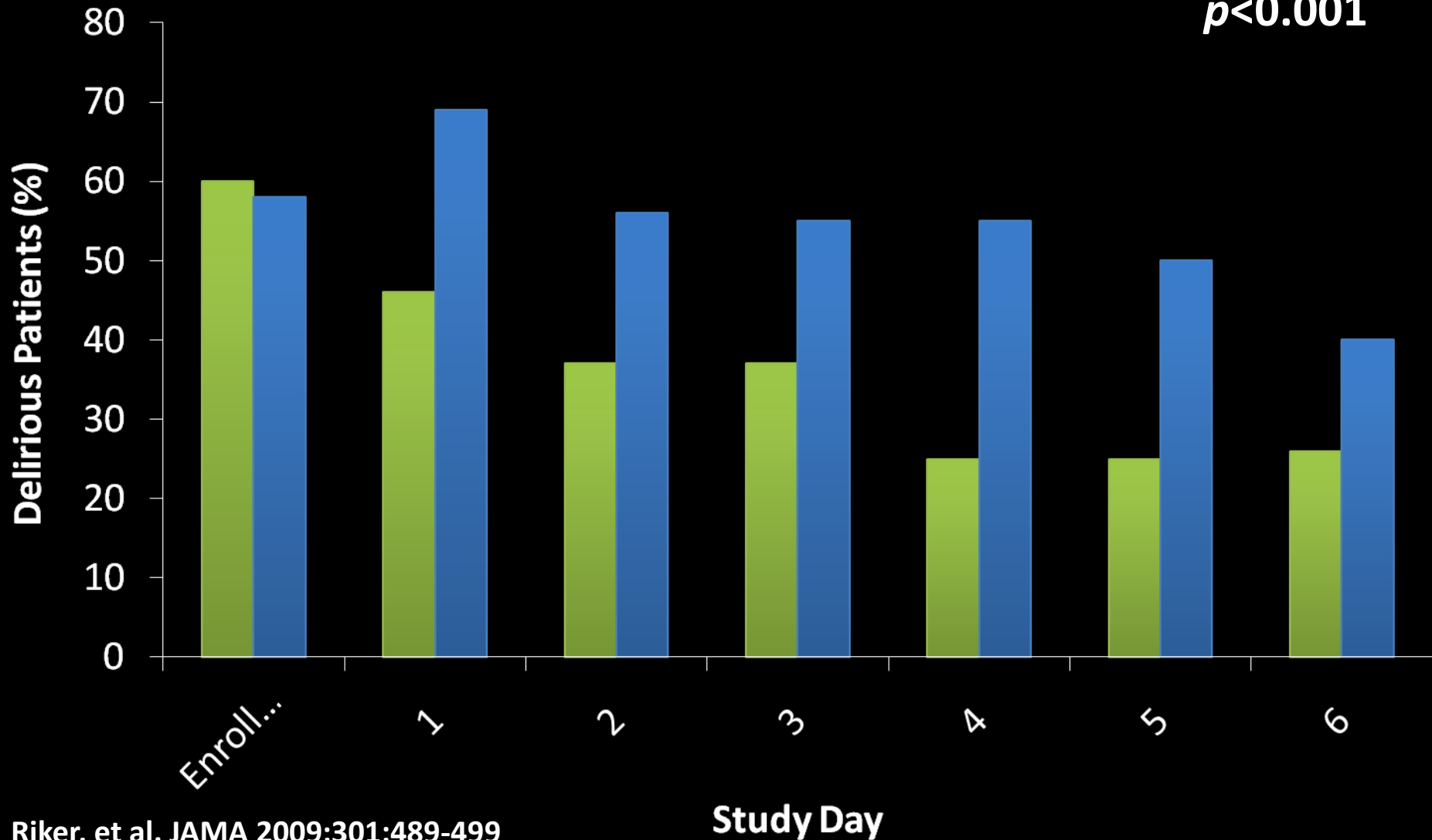
■ Dexmedetomidine ■ Lorazepam



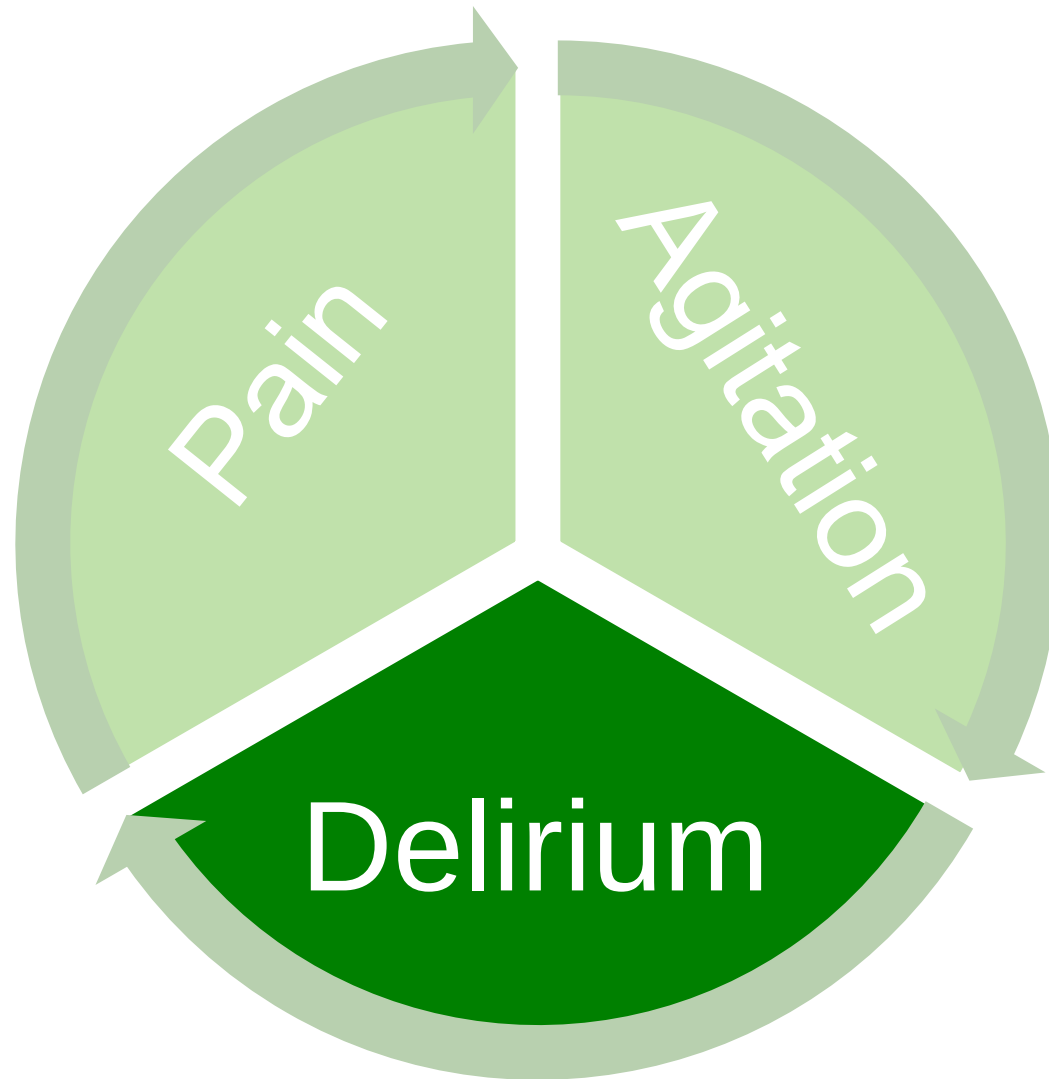
Daily Risk of Delirium in SEDCOM

■ Dexmedetomidine ■ Midazolam

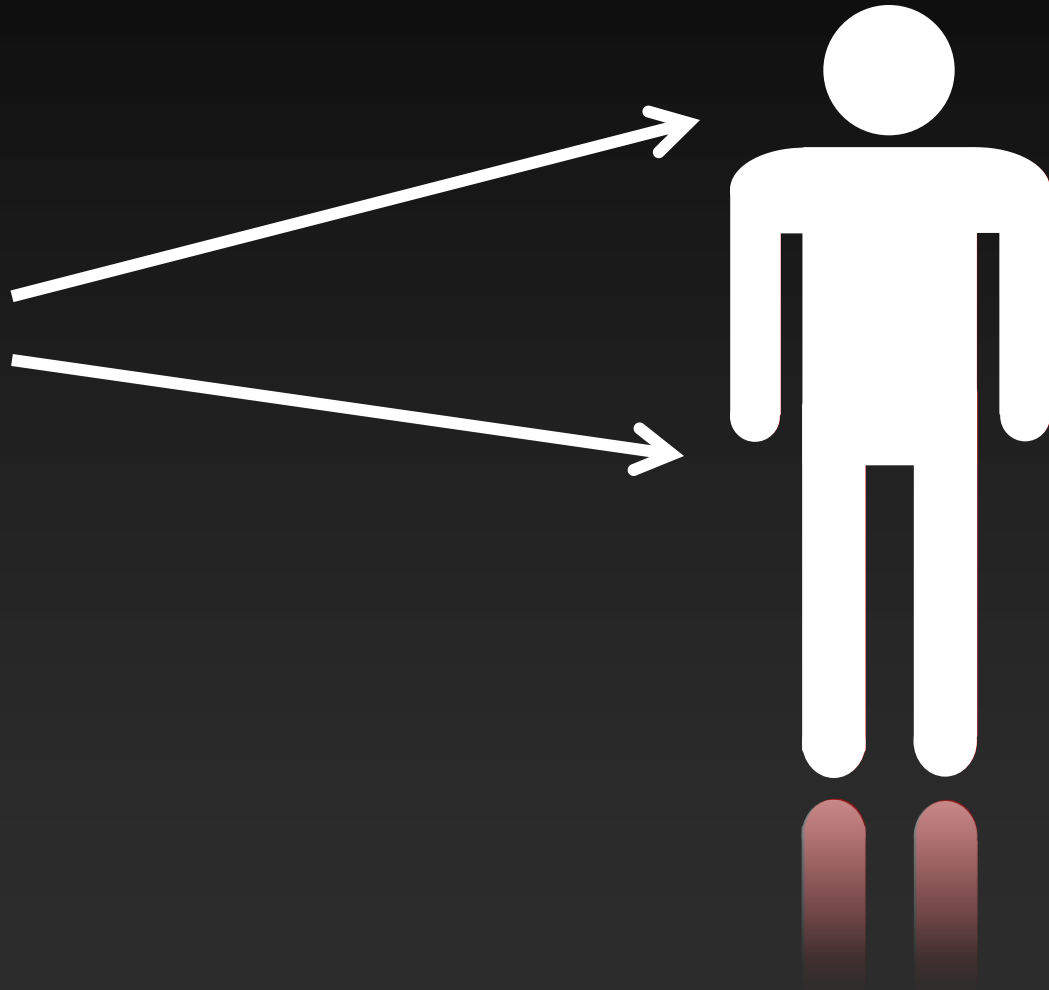
$p < 0.001$



Pain, Agitation, and Delirium Are Interrelated



**Critical
Illness**



Critical Illness

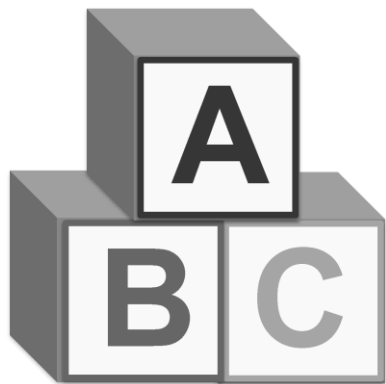


Delirium

ICU

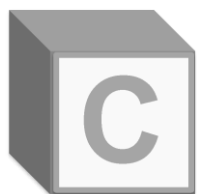
Acquired Weakness

Ely, et al., *JAMA* 2004; 291: 1753-62
Devlin et al., *Intensive Care Med* 2007; 35:2721-4
Bergeron et al., *Intensive Care Med* 2001; 27:859-64
Needham DM *JAMA* 2008; 300: 1685-94
DeJonghe, et al., *JAMA* 2002; 288: 2859-67



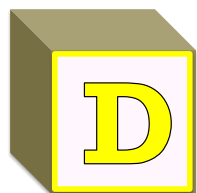
Awake and Breathing Coordination

- ↓ Duration of mechanical ventilation
- ↓ Duration of coma
- ↓ Mortality



Choose light sedation & avoid benzos

- ↓ Duration of mechanical ventilation
- ↓ Mortality
- ↓ Delirium



Delirium monitoring & management

- ↑ Delirium detection

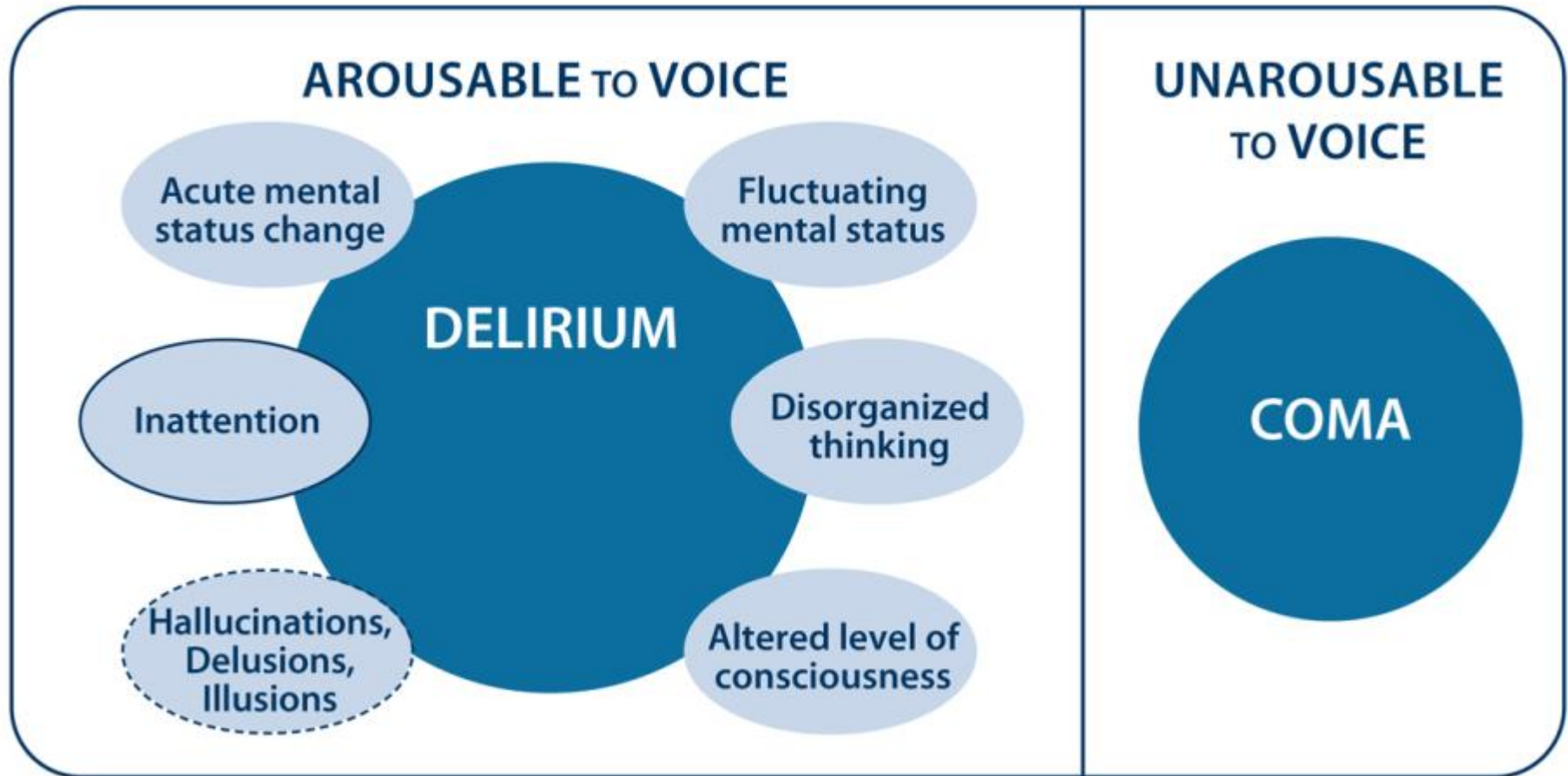


Early Mobility & Environment

- ↓ Duration of delirium
- ↓ Disability
- ↓ ICU Length of Stay
- ↓ Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Vasilevskis et al Chest 2010;138:1224-1233
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 2012;78:1026-33

Cardinal Symptoms of Delirium and Coma



2013 PAD Guidelines:

“We recommend routine monitoring
for delirium in adult ICU patients”

Grade 1B Recommendation

Crit Care Med. 2013;41:263-308

If delirium is not screened for using a validated delirium screening tool it is missed ~75% of time.

Inouye SK *Arch Intern Med.* 2001;161:2467-2473.

Devlin JW *Crit Care Med.* 2007;35:2721-2724.

Spronk PE *Intensive Care Med.* 2009;35:1276-1280.

van Eijk MM *Crit Care Med.* 2009;37:1881-1885.

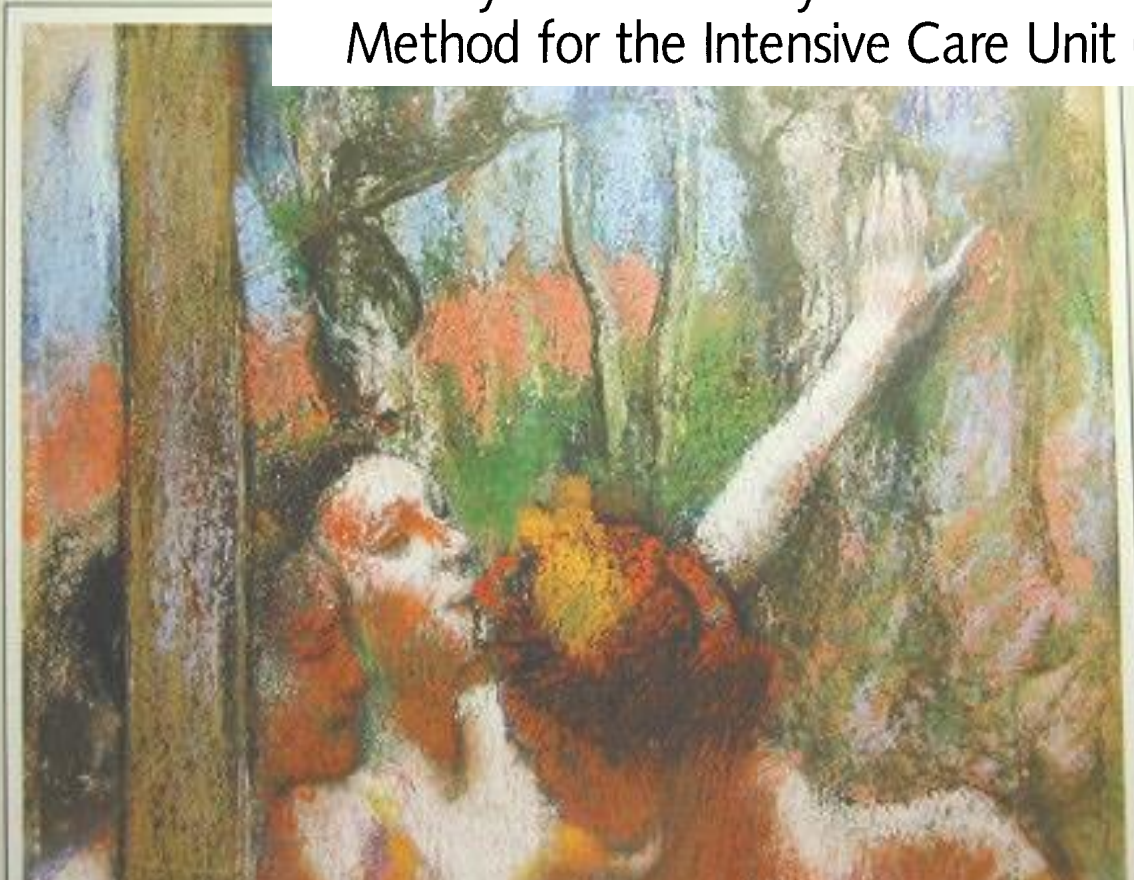
JAMA
The Journal of the American

**CARING FOR THE
CRITICALLY ILL PATIENT**

Ely EW, JAMA 2001;286:2703-10

Delirium in Mechanically Ventilated Patients

Validity and Reliability of the Confusion Assessment
Method for the Intensive Care Unit (CAM-ICU)



JAMA[®]

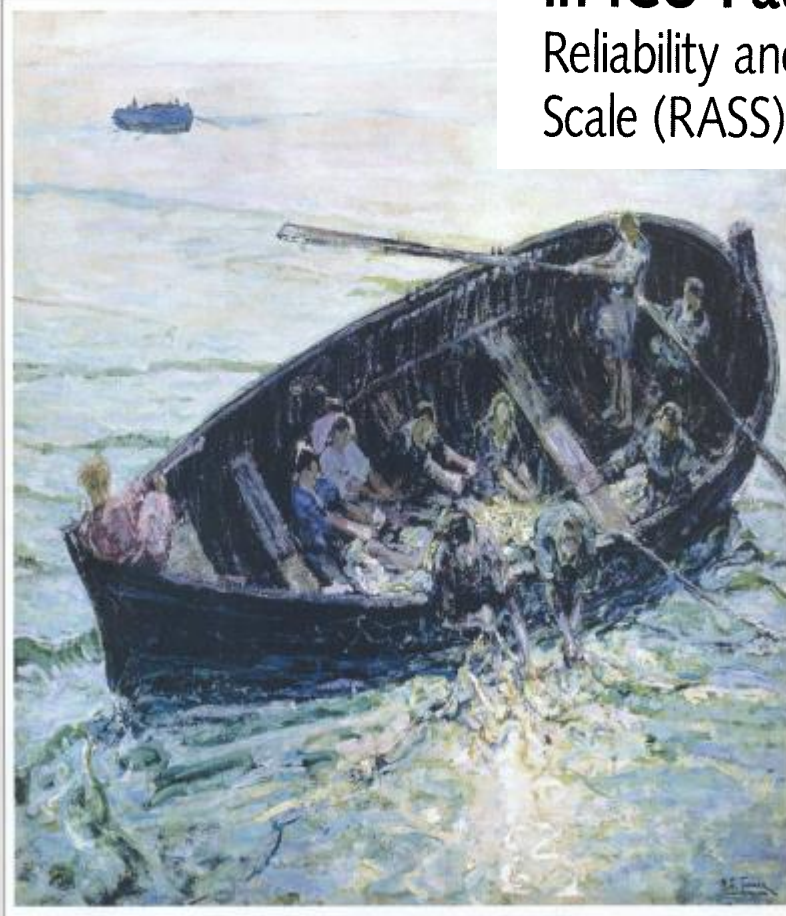
The Journal of the American Medical Association

**CARING FOR THE
CRITICALLY ILL PATIENT**

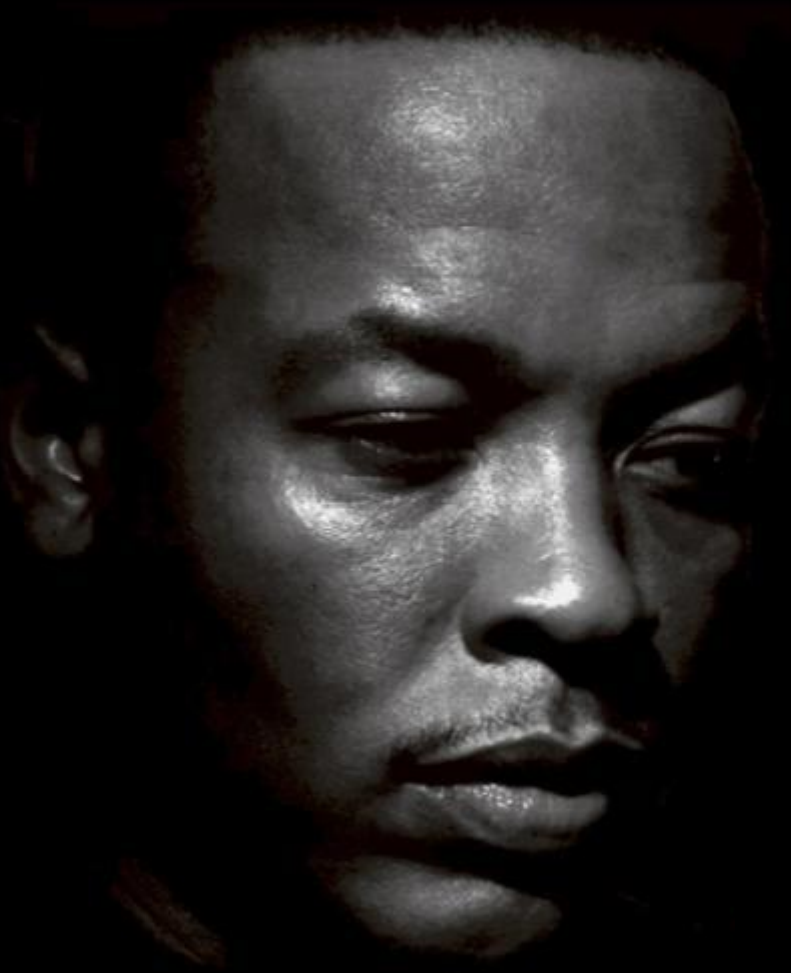
Ely EW, JAMA 2003;289:2983-91

Monitoring Sedation Status Over Time in ICU Patients

Reliability and Validity of the Richmond Agitation-Sedation Scale (RASS)



Don't forget about Dr. DRE



Diseases

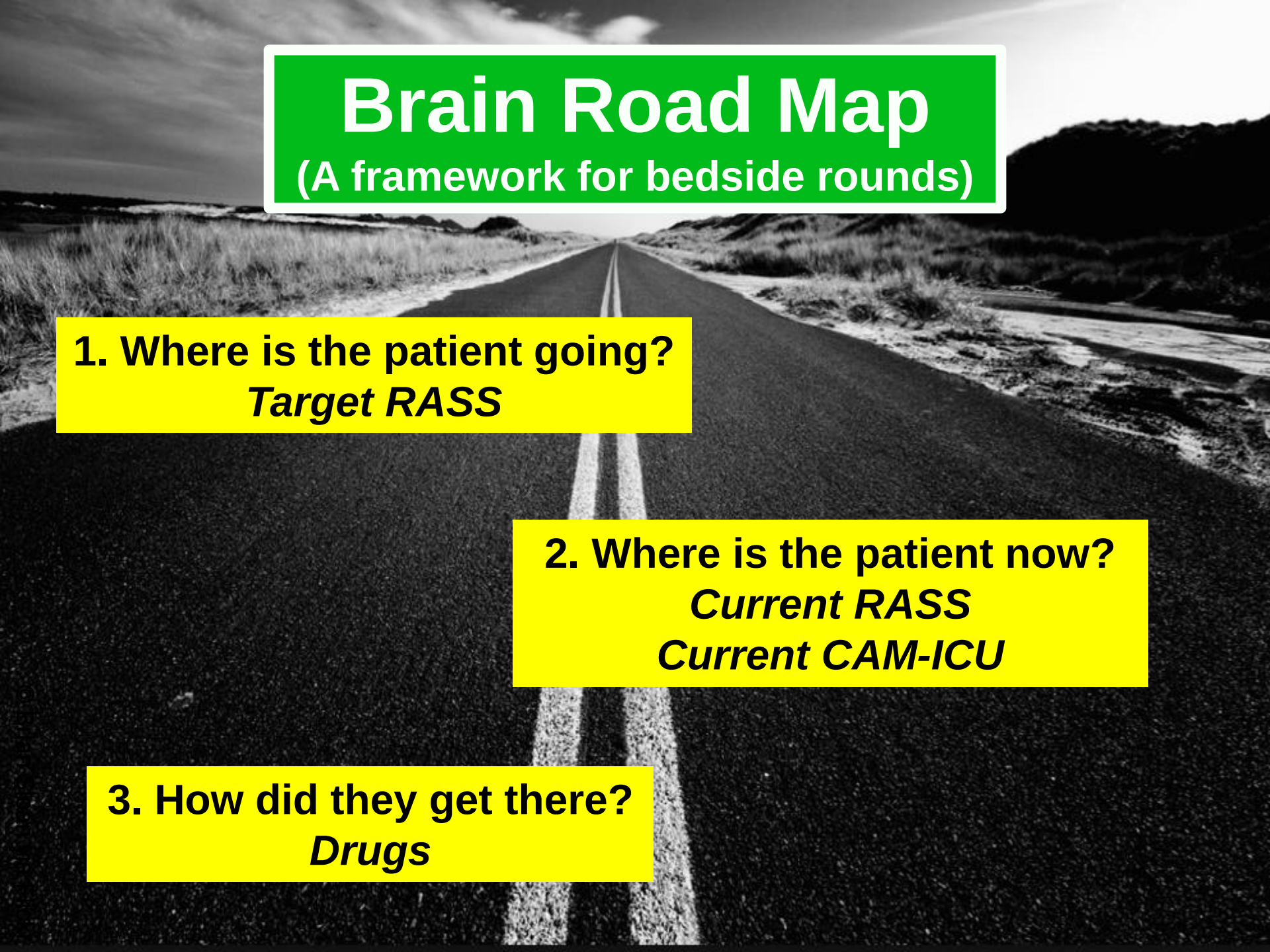
Sepsis, COPD, CHF

Drug Removal

*SATs and stopping benzodiazepines/
narcotics*

Environment

*Immobilization, sleep and day/night,
hearing aids, glasses, noise*



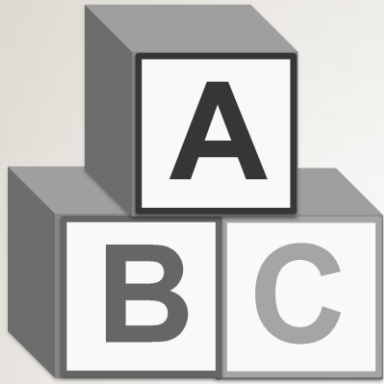
Brain Road Map

(A framework for bedside rounds)

1. Where is the patient going?
Target RASS

2. Where is the patient now?
Current RASS
Current CAM-ICU

3. How did they get there?
Drugs



Awake and Breathing Coordination

- ↓ Duration of mechanical ventilation
- ↓ Duration of coma
- ↓ Mortality



Choose light sedation & avoid benzos

- ↓ Duration of mechanical ventilation
- ↓ Mortality
- ↓ Delirium



Delirium monitoring & management

- ↑ Delirium detection

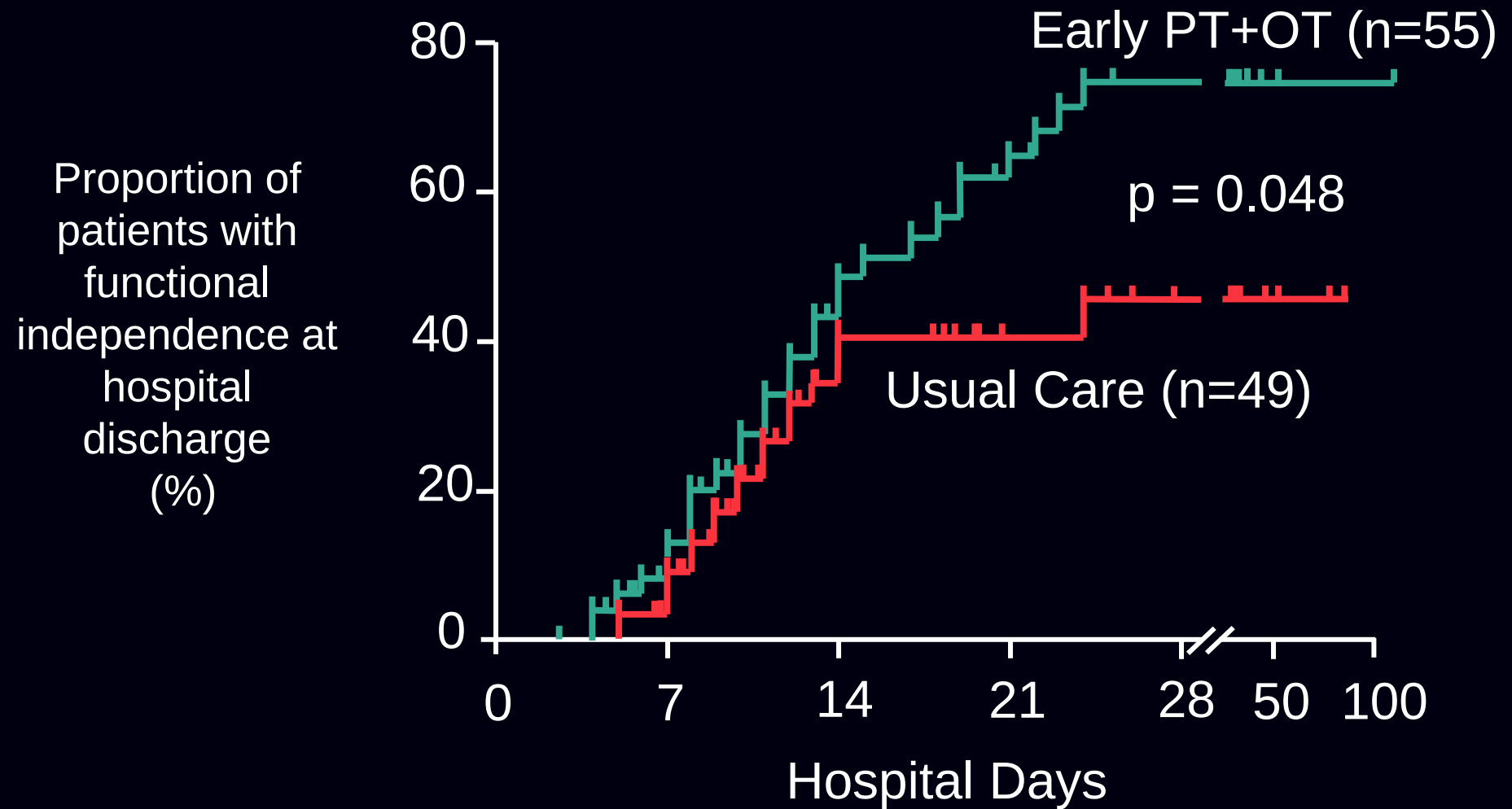


Early Mobility & Environment

- ↓ Duration of delirium
- ↓ Disability
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- ↓ Rehospitalization/Mortality

Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Vasilevskis et al Chest 2010;138:1224-1233
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 2012;78:1026-33

Early physical rehabilitation



Mobilization = Less Delirium

Variable	Intervention (n=49)	Control (n=55)	P-value
ICU/Hosp Delirium Days	2 days	4 days	0.03
Time in ICU with Delirium	33%	57%	0.02
Time in Hosp. with Delirium	28%	41%	0.01

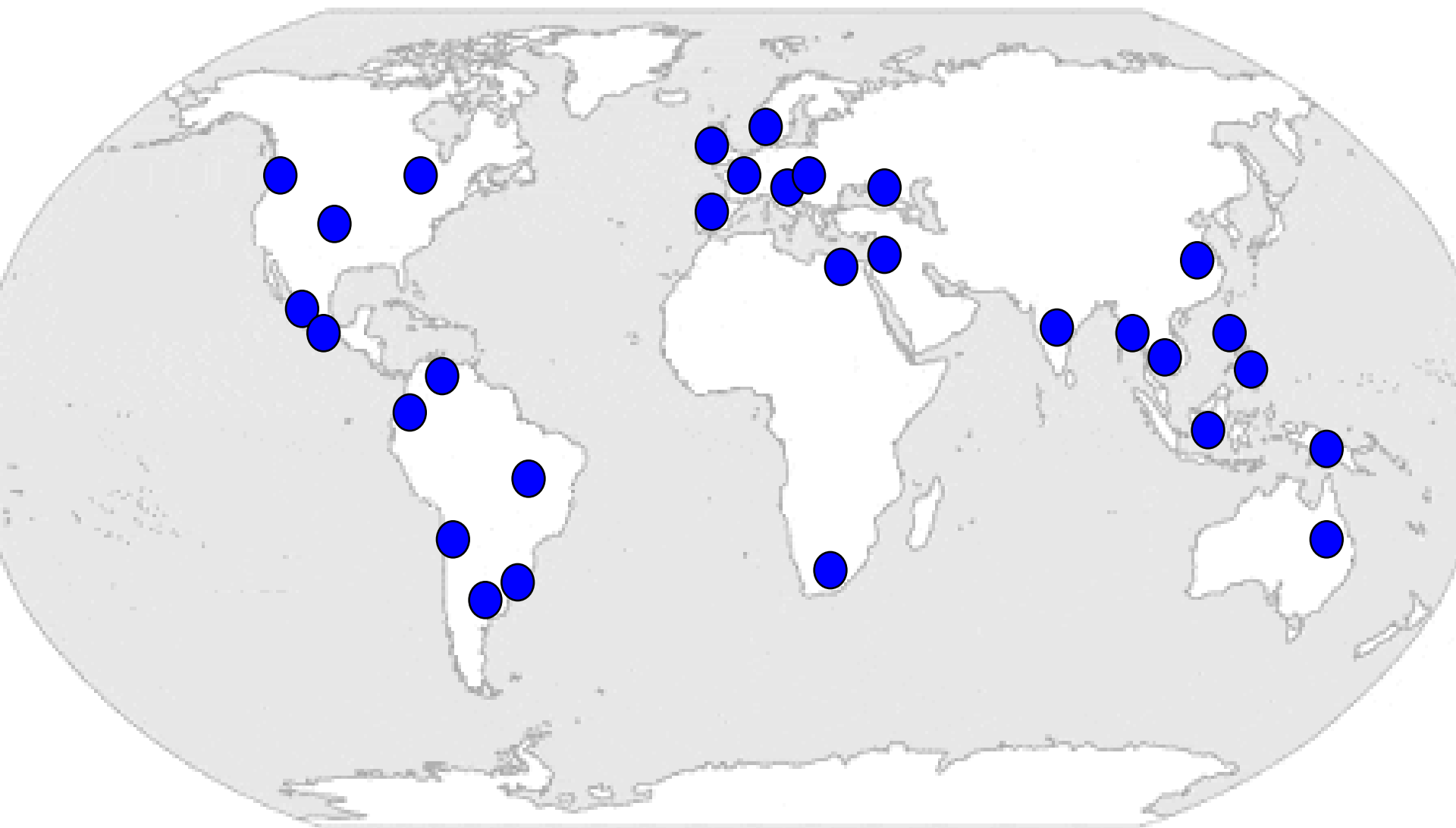
Mobilizing the Brain with Sudoku & Scrabble



Changing ICU Management Worldwide

Delirium Monitoring in ICUs Worldwide - 2012

(over 20 languages)



**““ I survived and that is the main thing.
And I am so grateful to God that I
survived and am now off all oxygen
and consider myself all well except
that I can't remember to take my
medications...**

-SB



Key Epidemiological Points:

- 1) Patients suffer from long-lasting and disabling aspects of critical illness that demand our attention as a medical community
- 2) Acquired or accelerated cognitive impairment is a major public health problem following ICU care for both the old and young
- 3) This cognitive impairment appears most pronounced in domains of executive dysfunction and memory
- 4) Frontal lobe and hippocampal atrophy are being consistently found in recent studies
- 5) This injury is likely distinct from or complementary to Alzheimer's pathology, though we are in our infancy in learning about this entity (e.g., large pathology study under review)
- 6) Delirium and drug exposure appear to be the most modifiable aspects of care, with need for more trials to delineate next steps

Key Management Points:

- 1) Establish an overarching protocolized approach to daily ICU patient management using 2013 PAD Guidelines
- 2) Assess & treat pain first (may be sufficient)
- 3) If patient remains agitated after adequately treating pain, use prn/bolus sedation initially, if frequent boluses (>3/hr) use continuous sedation
- 4) Avoid benzodiazepines in most patients
- 5) Turn off sedation daily and restart only if needed at lowest dose to maintain chosen target level of consciousness
- 6) Deep sedation (RASS -4/-5) appears harmful; target awake/alert
- 7) Screen for delirium (CAM-ICU or ICDSC); If delirious, first seek reversible causes and attempt non-pharmacologic management
- 8) Use the ABCDEs to improve outcomes for your patients

icudelirium.org

RESEARCH DESIGNED TO TURN
MIRRORS INTO WINDOWS



ICU Delirium and Cognitive Impairment Study Group: selected local members

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Live Board Review Session I
Saturday, August 10, 2013

1. A 45-year-old man who was recently treated for small cell lung cancer and a history of chronic obstructive pulmonary disease is admitted to the ICU because of acute dyspnea and severe chest pain. Arterial blood studies (with the patient breathing 60% oxygen by face mask) reveal PaO_2 of 48 mm Hg, PaCO_2 of 53 mm Hg, and pH of 7.35. A pulmonary arteriogram shows large pulmonary emboli, so he receives an anticoagulant. He soon begins to tire and continues to desaturate despite supplemental oxygen followed by noninvasive positive pressure ventilation (NIPPV). When it appears the patient will require intubation and mechanical ventilation, his spouse says that his living will states that he does not want "heroic measures," including mechanical ventilation. He expresses the desire to be kept comfortable without the "tight" oxygen mask and without any acceleration in the current level of life support. On being informed of the potential reversibility of his acute problem, he still refuses intubation in the presence of his spouse. Although the patient describes ongoing pain, neurologic assessment reveals no delirium and no evidence of altered decision-making capacity. Which of the following is the most appropriate course of action?

- a. Remove noninvasive ventilation, increase morphine, and provide supplemental oxygen
- b. Discontinue morphine and discuss his situation again when drug effect has abated
- c. Provide sedation and proceed with intubation
- d. Obtain a psychiatric consultation

2. A 68-year-old man with chronic obstructive pulmonary disease, hypertension, and hyperlipidemia is being weaned from mechanical ventilation. As part of a standardized weaning protocol, he is started on a spontaneous breathing trial. He initially tolerates the trial well, but later shows evidence of desaturation and agitation. He is given larger doses of lorazepam for sedation, and assist-control ventilation is resumed. The patient's current medications are metered-dose ipratropium/albuterol inhalers through the ventilator circuit; prednisone, 40 mg/day; lisinopril, 5 mg/day; and atorvastatin, 10 mg/day. The next day the patient is calm but confused. Which of the following instruments is most likely to be of value in evaluating the patient?

- a. Beck Depression Inventory
- b. Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)
- c. Folstein Mini-Mental State Examination (MMSE)
- d. Instrumental Activities of Daily Living Scale

3. A 69-year-old patient with diabetes is placed on mechanical ventilation for severe sepsis and acute respiratory distress syndrome due to community-acquired pneumonia. On day 1, he receives assist-control ventilation with FIO_2 of 70% and positive end-expiratory pressure (PEEP) of 12 cm H_2O ; by day 3, the FIO_2 is 45% and PEEP is 6 cm H_2O . He is on a propofol drip and has received intermittent fentanyl but now appears to be in no pain. His Richmond Agitation-Sedation Scale (RASS) score is -4, which indicates that he responds to physical, and not to verbal, stimulation. Which of the

following is the best course of action regarding weaning him from sedation and ventilation?

- a. Change his propofol drip to intermittent bolus sedation, and then change his ventilator to pressure support ventilation
- b. Completely stop sedation; if he wakes to verbal stimulation, put the ventilator on continuous positive airway pressure as a trial of spontaneous oxygenation and ventilation
- c. Switch from propofol to fentanyl as an analgesia-based sedation strategy to cover both anxiety and pain, and reduce PEEP to 5 cm H₂O
- d. After further recovery, gradually reduce both the sedation dosage and the ventilatory support to avoid abrupt changes and the risk of anxiety

4. A 45-year-old man is admitted to the ICU after a fall related to alcohol intoxication. He is sedated with haloperidol and lorazepam, with fentanyl for analgesia. The Richmond Agitation-Sedation Scale goal is –1. The goal of this level of sedation is:

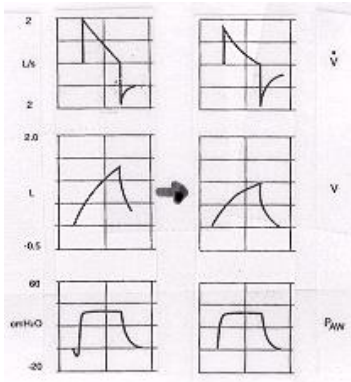
- a. Drowsiness
- b. Deep sedation
- c. Alertness
- d. Moderate sedation

5. A 69-year-old woman with a long history of arthritis, peptic ulcer disease, and remote abdominal surgery developed an acute bowel obstruction and underwent laparotomy for release of adhesions. Following postoperative hypoventilation with a PCO₂ of 55 mm Hg, she was extubated successfully on postoperative day 2. Two days later, as she was recovering in the ICU, she developed fluctuations in her mental status and inattention. Her physician thought that she was developing delusions and wrote in her chart, “She is hallucinating and pulling at her lines, asking to leave the hospital despite being reassured that she needs to stay for recovery.” Her arterial blood gas results were normal. Subsequent notes by multiple personnel indicated that she had no hallucinations or delusions but was having fluctuations in her level of consciousness and was unable to maintain attention. She had no focal motor or sensory abnormalities. Which of the following statements is the most appropriate guide in determining whether she is definitively delirious?

- a. She meets the criteria for delirium because of her well-documented hallucinations and delusions
- b. The cornerstone of her diagnosis rests on her inability to maintain attention
- c. Her agitation is most worrisome because hyperactive delirium has a worse prognosis than hypoactive delirium
- d. Delirium is an all-or-none phenomenon, and the duration of this form of brain dysfunction is not important

6. A patient recovering from acute respiratory distress syndrome is receiving pressure assist-control ventilation and is triggering virtually all of the ventilator breaths (left panel below). An upper endoscopy is required to evaluate new bleeding in the upper

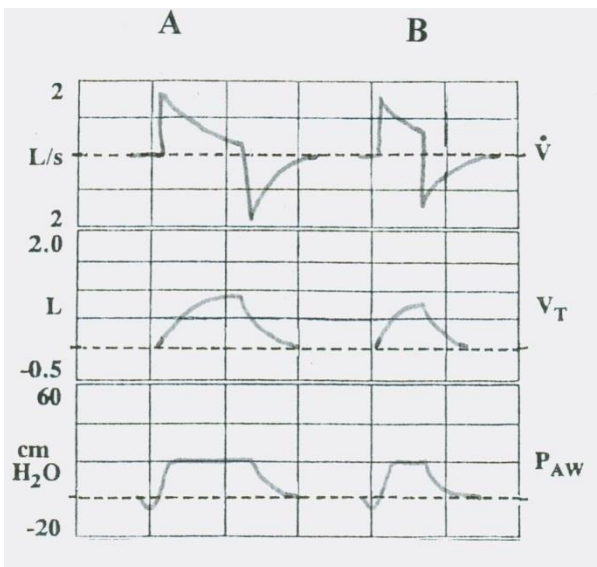
gastrointestinal tract, and a neuromuscular blocker is administered to facilitate this procedure. The ventilator graphics abruptly change to those shown in the right panel (below).



Which of the following is the best explanation for the change in the graphics?

- a. Loss of spontaneous effort
- b. Idiosyncratic reaction to neuromuscular blocker causing flash pulmonary edema
- c. Bronchospasm
- d. Mucous plugging

7. In the Figure (below), 2 pressure support breaths in the same patient are depicted. What has occurred between breath A and breath B?



- a. The inspiratory time setting has lengthened
- b. The patient's compliance has worsened
- c. The volume backup setting has increased
- d. The flow cycle percentage criteria have been increased
- e. The mandatory breath rate has increased

8. A 56-year-old man is intubated and placed on mechanical ventilation for acute respiratory distress syndrome (ARDS) after a seizure and massive aspiration. His lactate level is normal, he is hemodynamically stable, and he has adequate urine output. According to findings of a 2006 ARDS Network fluid management trial, the best fluid management strategy (i.e., liberal fluids prioritizing cardiac filling versus conservative fluids prioritizing “dry lungs”) and the best method of monitoring (i.e., central venous catheter [CVC] versus pulmonary artery catheter [PAC]) for this patient are:

- a. Conservative fluids, monitoring with either CVC or PAC
- b. Conservative fluids, monitoring with CVC only
- c. Liberal fluids, monitoring with either CVC or PAC
- d. Liberal fluids, monitoring with CVC only

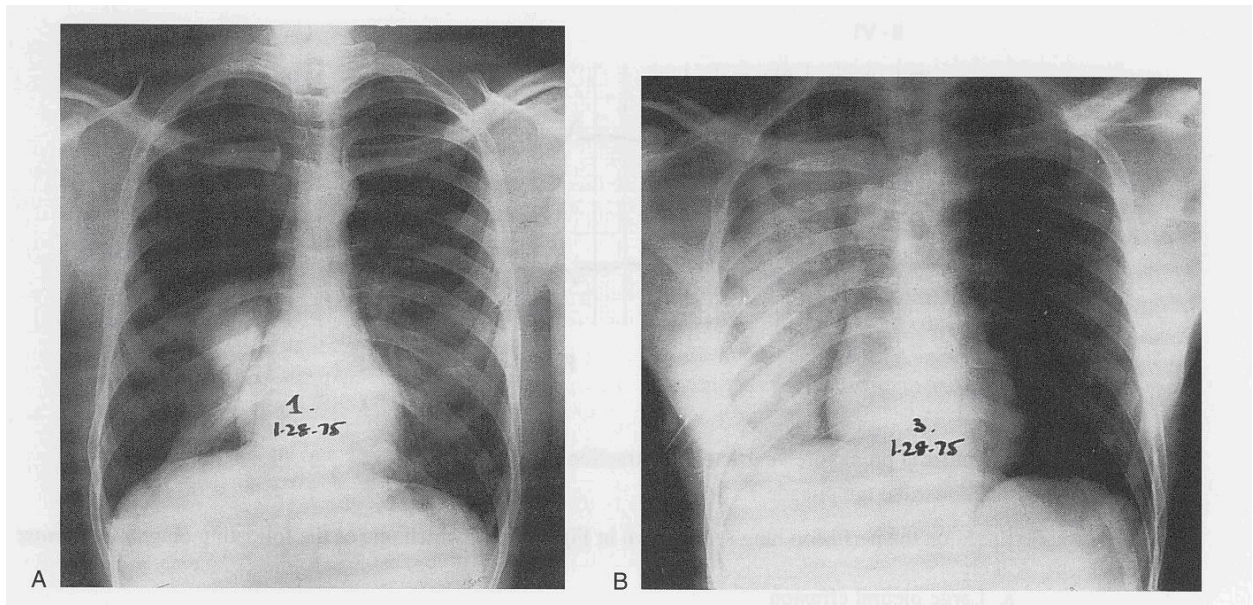
9. In a morbidly obese patient receiving mechanical ventilation, which of the following best characterizes the status of the end-inspiratory airway plateau pressure (Pplat) as an indicator of end-inspiratory transpulmonary pressure?

- a. A reasonable estimate of end-inspiratory transpulmonary pressure
- b. A gross underestimate of end-inspiratory transpulmonary pressure
- c. A gross overestimate of end-inspiratory transpulmonary pressure
- d. Unrelated to end-inspiratory transpulmonary pressure

10. A patient with chronic obstructive pulmonary disease has received a single lung transplant. Pneumonia has developed in the transplanted left lung, requiring mechanical ventilatory support. A double-lumen tube is inserted to ventilate each lung separately. Which of the following is the most important strategy for setting up the two ventilators?

- a. Tidal volume settings should be 6 mL/kg ideal body weight in each lung
- b. Positive end-expiratory pressure should be equal in both lungs
- c. Respiratory rate should be synchronized in the two lungs
- d. A plateau pressure of 30 cm H₂O should be maintained in both lungs

11. The figures (below) show radiographs before and after a thoracostomy tube insertion for a large pneumothorax in a hemodynamically stable patient.



Which of the following most correctly describes the chest radiograph findings?

- a. Tension pneumothorax on the left side
- b. Near-total right lung atelectasis
- c. Evidence that the original pneumothorax may have been long-standing
- d. Pneumopericardium

12. A 50-year-old woman has severe facial trauma following a motor vehicle crash. She is obtunded with an RR of 40/min. Arterial blood gas measurements reveal pH of 7.20, PaCO_2 of 65 mm Hg, and PaO_2 of 60 mm Hg on high-flow face mask oxygen. The decision is made to intubate the patient for airway protection and mechanical ventilation. Under these circumstances, which of the following is the best method for endotracheal intubation?

- a. Fiberoptic nasal intubation
- b. Oral intubation with in-line cervical spine stabilization
- c. Cricothyrotomy
- d. Blind nasotracheal intubation

13. A 45-year-old man with an acute, severe asthma attack is admitted to the ICU. He has a history of hypertension and glaucoma. Chest radiography reveals hyperinflation and an absence of infiltrates. His medical therapy in the emergency department included continuous aerosolized albuterol as well as IV methylprednisolone, 125 mg. His peak expiratory flow rate is unimproved at 80 L/min (personal best, 450 L/min). Which of the following is most appropriate to add as additional medical therapy?

- a. Nebulized ipratropium by face mask
- b. IV magnesium sulfate
- c. Broad-spectrum antibiotics targeting community-acquired respiratory pathogens
- d. Inhaled corticosteroids

14. A 42-year-old woman with alcohol dependence, malaise, confusion, jaundice, and severe liver disease requires mechanical intubation for airway protection. She is given ceftriaxone, as well as propofol for sedation. Because of the poor likelihood of recovery, she is listed for liver transplant. After infusion of fresh frozen plasma and 5,000 µg of recombinant factor VIIa, an intracranial pressure monitor is placed with an opening pressure of 10 mm Hg (normal). A repeat international normalized ratio is 2.0, creatinine level is 3.0 mg/dL, and hemoglobin is 12 g/dL. Three hours later, the nurse says the intracranial pressure is 30 mm Hg with a mean arterial pressure of 85 mm Hg. Physical examination reveals hyperreflexia throughout and minimal response to sternal rub with intact pupillary reflexes. The patient is lying flat. Arterial blood gas results show pH of 7.43, PaCO₂ of 28 mm Hg, and PaO₂ of 72 mm Hg on 30% FIO₂. Which of the following is the best next step?

- a. Place catheter to initiate hemodialysis
- b. Administer dexamethasone
- c. Elevate the head of the bed to 30°
- d. Cool the patient to 33°C (91.4°F)

15. A 23-year-old woman presents with a 3-day history of nausea, vomiting, and abdominal pain. She underwent sinus surgery 2 weeks ago that was complicated by severe facial pain leading to prescriptions of amoxicillin/clavulanate for 10 days and 40 tablets of acetaminophen/hydrocodone, 1 tablet every 4 to 6 hours.

She took all of the acetaminophen/hydrocodone tabs including a refill of 40 more tablets. During the past 5 days, she has also taken extra-strength, over-the-counter acetaminophen, 500 mg tablets every 4 hours for a severe frontal headache and had several beers since she finds it difficult to eat and keep food down.

In the emergency department, BP is 80/40 mm Hg with a pulse rate of 100/min. She is sleepy but arousable with no asterixis and mild epigastric tenderness. Initial laboratory results are as follows: aspartate aminotransferase, 3,000 U/L; alanine aminotransferase, 4,000 U/L; alkaline phosphatase, 100 U/L; bilirubin, 4.0 mg/dL; international normalized ratio, 3.0; complete blood count, normal; amylase, 200 U/L; lipase, 300 U/L; creatinine, 2 mg/dL; and serum bicarbonate, 14 mEq/L. Arterial blood gas results show pH of 7.35, Paco₂ of 35 mm Hg, and Pao₂ of 90 mm Hg on room air.

Serum acetaminophen level is less than 10 µg/mL, a urine toxicology screen shows diphenhydramine, and liver ultrasonography findings are normal.

The most likely diagnosis is:

- a. Alcoholic hepatitis
- b. Acetaminophen overdose (nonintentional)
- c. Choledocholithiasis
- d. Amoxicillin/clavulanate hepatotoxicity
- e. Severe pancreatitis

Difficult Management Problems: ARDS, Mechanical Ventilation, Weaning



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Format for Cases/Questions

- NOTE: This set of questions is about a single patient followed on successive days
- Each day presents
 1. the TEACHING POINT
 2. followed by a QUESTION
 3. followed by an OBJECTIVE
 4. followed by the ANSWER with a narrative

TEACHING POINT 1

A 71-year-old woman is brought to the emergency department from a nursing home because of confusion, fever, and flank pain. Temperature is 38.5 C (101.3 F), pulse rate is 123 per minute, respirations are 27 per minute, and blood pressure is 82/48 mm Hg. Physical examination reveals dry mucous membranes, costovertebral tenderness, poor skin turgor, and no edema. Leukocyte count is 15,600 and urinalysis shows 50–100 WBCs with many bacteria. The patient has a metabolic acidosis and high lactate levels believed due to septic shock.

Question 1

In conjunction with appropriate antibiotics, which of the following choices is most likely to result in improved survival for this patient (**Single Answer**)?

- (A) 25% albumin infusion
- (B) Aggressive and early fluid resuscitation with crystalloid
- (C) Maintaining a hemoglobin level above 12 mg/dl
- (D) Maintaining a PaCO_2 below 50 mm Hg
- (E) IV steroids

OBJECTIVE 1

- To emphasize that aggressive fluid resuscitation is a life saving and time sensitive intervention for severe sepsis patients, regardless of the type of monitoring device

Answer to TEACHING POINT 1

The correct answer is (B) Aggressive fluid resuscitation using crystalloid with the goal of resolution of lactic acidosis within 6 hours. This patient has severe sepsis presumptively from pyelonephritis. The point here is that “timing” of resuscitation matters to survival. In a landmark study by Rivers et al., early goal directed therapy (EGDT) that interventions (fluid, blood, dobutamine, etc) delivered within the first 6 hours to maintain a central venous O₂ saturation of >70% and to effect resolution of lactic acidosis resulted in higher survival rates than more delayed resuscitation attempts. Indeed, over the first 72 hours those in the control arm received the same quantity of fluid for their resuscitation (~13 liters), but they had a significantly higher likelihood of dying by discharge or 60 days. The other answers are all invoking interventions that do not increase survival in severe sepsis. Crystalloid is given much more frequently than colloid, and there are no data to support routinely using colloid in lieu of crystalloid (see the SAFE study), especially in patients who are so obviously volume depleted such as this patient. Giving blood may be part of resuscitation for anemic patients in shock, but going to levels above 12 is not supported. In stable patients who are not in shock, Hebert and colleagues showed that a transfusion threshold of 7 g/dl that is an acceptable “conservative” approach in ICU patients, but this does not apply to the early period of EGDT. Steroids will also be discussed.

TEACHING POINT 2

Despite your intentions, this same 71-year-old woman receives only 2 liters of fluid over 6 hours in the ED while awaiting ICU transfer and then resuscitation is ramped up considerably with 8 liters of normal saline and a norepinephrine drip, but the patient develops ARDS and oliguric renal failure by the next morning.

Question 2

In such patients, placement of a pulmonary artery catheter to obtain the PAOP (i.e., wedge pressure), as opposed to management using CVP, is most likely to result in which of the following (**Single Answer**)?

- (A) Decreased 28-day mortality
- (B) Decreased length of ICU stay
- (C) Decreased incidence of congestive heart failure
- (D) No identifiable benefit
- (E) Decreased incidence of renal dysfunction

OBJECTIVE 2

To understand that placement of a pulmonary artery catheter has been recently shown in multiple studies to offer no identifiable benefit in the routine management of ARDS patients

Answer to TEACHING POINT 2

The correct answer is (D) No identifiable benefit. None of the other answers is correct. Over the past 30 years, the pulmonary artery catheter (PAC) became a widely used hemodynamic monitoring device in the management of critically ill patients, though doubts exist about its utility and safety. Four large, multi-center, randomized controlled trials of critically ill ICU patients have shown no mortality or outcomes benefits from management guided by placement of a PAC. **A PAC is no better than a CVP in managing fluid status in ARDS/Sepsis.** While the PAC may still have a role in a selected minority of patients, routine placement of these devices is not appropriate. Whether care was protocolized with specific hemodynamic goals or not, and regardless of admission diagnosis or hemodynamic profile (e.g., cardiogenic shock vs. sepsis vs. ARDS), there was no identifiable advantage in any of these trials to having PAC-guided therapy.

TEACHING POINT 3

This same 71 year-old woman with septic shock developed diffuse bilateral infiltrates consistent with ARDS and progressive hypoxemic respiratory failure ($P/F < 100$) necessitating mechanical ventilation. The patient was placed on Assist Control ventilation with V_t of 8ml/kg, PEEP 12, 70% FiO_2 , P_{plat} of 41, and V_E of 15 l/min. She stabilizes to some degree but her O_2 saturations are 90% and she is breathing 28/min without breath stacking. Your partner asks you to increase the tidal volume, increase the PEEP to “high” levels, and to perform recruitment maneuvers.

Question 3

According to the latest evidence in the literature, which of the following statements is most appropriate at this time regarding ventilator management (**Single Answer**)?

- (A) Use recruitment maneuvers to wean FiO_2
- (B) Increase PEEP to 18 cm H_2O
- (C) Reduce V_t to 6 ml/kg predicted body weight
- (D) Increase V_t to 10 ml/kg predicted body weight
- (E) Change the patient to bi-level ventilation

OBJECTIVE 3

- To review the best evidence regarding “dosing air” so as to optimize support without causing harm, as well as to discuss issues related to physiology and clinical course.

Answer to TEACHING POINT 3

The correct answer is (C) Reduce V_t to 6 ml/kg ideal body weight, as per the ARDS network's trial showing a 25% relative risk reduction in mortality (10% ARR, NNT 10). Using normal tidal volume indexed to predicted body weight improves survival even though it temporarily makes physiology look worse. PEEP within broad ranges doesn't alter outcome even though it improves oxygenation. As studied thus far (Gattinoni NEJM and Mancebo AJRCCM), randomized controlled trials have shown that recruitment maneuvers do not improve survival. Bi-level ventilation may be fine here but there are not data to support this mode over other standard modes such as volume A/C. Regarding breath stacking, which this patient did NOT have, the following is good to remember: When on A/C some patients stack breaths and the ARDSNET protocol was to increase V_t by up to 2 ml/kg - usually only 1 ml/kg is needed and even then, for only a while. Lastly, remember that improved oxygenation does not equate to survival

Additional data

The patient's arterial blood gas was NORMAL on 0.70 FiO₂ using assist control with a set rate of 22, V_t of 520 ml, and PEEP of 10 cm H₂O (pH 7.39, PaO₂ of 71, PaCO₂ of 42). Plateau airway pressure (P_{plat}) was 41 cm H₂O.

- Patient's predicted (i.e., ideal) body weight is 50 kg; her actual body weight is 65 kg.
- Ideal Body Weight (kg) formulae used in ARDS network trial:
- Male = $50 + 2.3 (\text{height in inches} - 60)$
- Female = $45.5 + 2.3 (\text{height in inches} - 60)$
- V_t was adjusted to ~300 ml and resultant P_{plat} was 29 cm H₂O (going lower may be even better – discuss)

TEACHING POINT 4

It is now day 4, and this same patient with ARDS and sepsis is out of shock and off vasopressors. She remains heavily sedated and on the ventilator. You are not sure of her fluid status, but she is clinically very edematous though oliguric.

Question 4

For this patient who is now stabilized and out of shock, with the ventilator being gradually reduced, which of the following steps in management have been shown to be APPROPRIATE (Single Answer):

- (A) Avoid diuretics and keep CVP >12 due to oliguria
- (B) Give diuretics and minimize fluids to goal CVP < 4
- (C) Transfuse the patient to maintain Hgb levels of 10
- (D) Start steroids for late phase ARDS
- (E) Once the patient passes an SBT, discontinue sedation

OBJECTIVE 4

- To discuss advances in our understanding of hemodynamic and medical management of ARDS and sepsis patients once they are stabilized and out of shock.

Answer to TEACHING POINT 4

The only correct answer is (B) Give diuretics and minimize fluids to $\text{CVP} < 4$. While early aggressive fluid resuscitation in shock is important, after reversal of shock, fluid removal (i.e., conservative or “dry” approach) improves physiology, shortens time on the ventilator, and survival moves in a favorable direction. Remember that “dry” in the FACTT was very dry, with a CVP of 4 mm Hg. A conservative transfusion threshold of ~ 7 is appropriate in most patients as long as there has been no active myocardial ischemia during hospitalization. Furthermore, once ARDS/sepsis patients are stabilized & out of shock, both PACs and liberal fluid management each separately contribute to substantial increases in numbers of patients transfused and average number of transfusions per patient. Steroids given between 7-14 days in ARDS may temporarily improve some physiology but not survival; later steroids are harmful. Discontinuing sedatives daily will improve outcomes of ventilator, ICU, and hospital length of stay.

TEACHING POINT 5

Two days later, the patient appears comfortable on 45% FiO_2 and low PEEP with SaO_2 of 90%. She is evaluated with an SBT (CPAP without PSV) and breathes easily for 30 minutes and is then extubated. Within the next 24 hours, the patient develops obvious respiratory distress without stridor. She desaturates to 85% and is diaphoretic with shallow breaths. She is placed on 5 cm H_2O CPAP initially, which is titrated to 10/5 cm H_2O BIPAP over the ensuing 4 hours because she is continuing to have trouble with tachypnea and small tidal volumes.

Question 5

This patient passed an abbreviated SBT but is now failing extubation. Which of the following statements is **TRUE** (Single Answer)?

- (A) It was inappropriate to try an SBT with SaO₂ of 90%
- (B) Protocols w/ SBTs shorten ~0.5 days off vent duration
- (C) Use clinical gestalt to determine who qualifies for SBTs
- (D) NIPPV is safe for stable COPD patients failing SBTs
- (E) NIPPV should be used for post-extubation resp distress

OBJECTIVE 5

- To review salient points about using SBTs in the context of protocolized weaning and to discuss appropriate use of NIPPV in common scenarios of liberating patients from mechanical ventilation.

Answer to TEACHING POINT 5

The only correct answer is (D) NIPPV is safe for stable COPD patients failing SBTs. Protocols using SBTs for patients with stable oxygenation result in patients getting off the ventilator on average about 2 days earlier than those not using SBTs. Using clinical gestalt to determine who will “pass an SBT” is notoriously fraught with error. One third of those who fail an SBT do so between 30 minutes and 2 hours. NIPPV may be useful as an immediate bridge post extubation for patients with chronic lung disease (e.g., COPD) who are stable but failing SBTs. However, for patients who pass an SBT and then go on to fail extubation, 2 recent studies failed to show significant outcomes benefits with the use of NIPPV for treatment of post-extubation respiratory distress. The larger of the two studies exposed a potential risk of increased deaths using NIPPV routinely for post-extubation respiratory failure.

Question 6

Which of the following statement is **TRUE (Single Answer)** about the Berlin Definition of ARDS for this patient who had a P/F ratio of ~85 at intubation and also had AKI and shock?

- (A) This is categorized as moderate ARDS
- (B) Because she had urosepsis, this would not be ARDS
- (C) Her predicted hospital mortality would be less than 20%
- (D) We need a Wedge pressure to determine if ALI is present
- (E) None of the above are true

OBJECTIVE 6

- To review salient points about BERLIN
Definition of ARDS within the context of this
particular patient example.

Answer to TEACHING POINT 6

The correct answer is (E), none of the above. This patient had severe ARDS at intubation (P/F is less than 100 on a PEEP of 5 or greater (her PEEP of 12). The diagnosis of ARDS doesn't hinge on the source of sepsis or injury. The Berlin Clinical Prediction Rule showed that severe ARDS had a mortality of 45%, and this patient has septic shock, AKI, and severe ARDS at least as organ dysfunction. The Berlin definition eliminated the PCWP as a component of the diagnosis and replaced it with more practical exclusion of CV disease. Thus, none of the options offered as answers were true except E.

Question 7

In accordance with the 2013 SCCM Sepsis Guidelines for management of patients such as this, the literature supports which of the following statements as **GRADE 1** (highest level) (**Single Answer**)?

- (A) Plateau Pressure should be maintained <30 cm H₂O
- (B) Ventilator weaning protocols with SBTs
- (C) Sedation protocols and minimization of sedation
- (D) All of the above
- (E) None of the above

OBJECTIVE 7

- To review salient points from the literature as reviewed and recommended by the 2013 Surviving Sepsis Campaign guidelines of the SCCM

Answer to TEACHING POINT 7

The answer is D, are all Grade 1 (highest) level recommendations. The addition of the B and C answers as Grade 1 recommendations indicates the logical overlap that was finally accomplished between the Sepsis and the PAD (pain/agitation/delirium) guideline committees. The literature between the two areas are complementary and must be applied across salient patient types.

Question 8

Which of the following statements regarding management of this patient with severe ARDS is **TRUE (Single Answer)**?

- (A) Neuromuscular blockade should be provided for mild, moderate, and severe ARDS now
- (B) HFO is an early choice as established by recent RCTs
- (C) Prone positioning is an established alternative management strategy but only for severe ARDS
- (D) Corticosteroids should be started early and often
- (E) Early tracheostomy is a proven way to reduce LOS and mortality at 1 year.

OBJECTIVE 8

- To review salient points about mechanical ventilation management in ARDS patients.

Answer to TEACHING POINT 8

The correct answer is (C), prone positioning is established for SEVERE ARDS. The Guerin study in the NEJM 2013 used a P/F <150 (slightly different than the more strict Berlin cutoff of 100) and 60% or more FiO₂ to demonstrate a large survival advantage (HR 0.4 for 90-day mortality). The proning was used for at least 16 hours/day and was stopped when P/F $\geq$ 150 on PEEP $\leq$ 10 and FiO₂ $\leq$ 60%. NMB is only supported for severe ARDS and certainly not mild (moderate in gray zone). HFO was disproven as an alternative in two 2013 NEJM studies called OSCAR and the CCCTG trial. Steroids remain controversial at best as standard management for ARDS depending on timing and severity and response to other treatments. Early tracheostomy is not advantageous for patients on mechanical ventilation in terms of LOS, survival, and most other outcomes except perhaps as a way of reducing sedation modestly (but that can be done without the trach).

Problems in Mechanical Ventilation

Neil MacIntyre MD

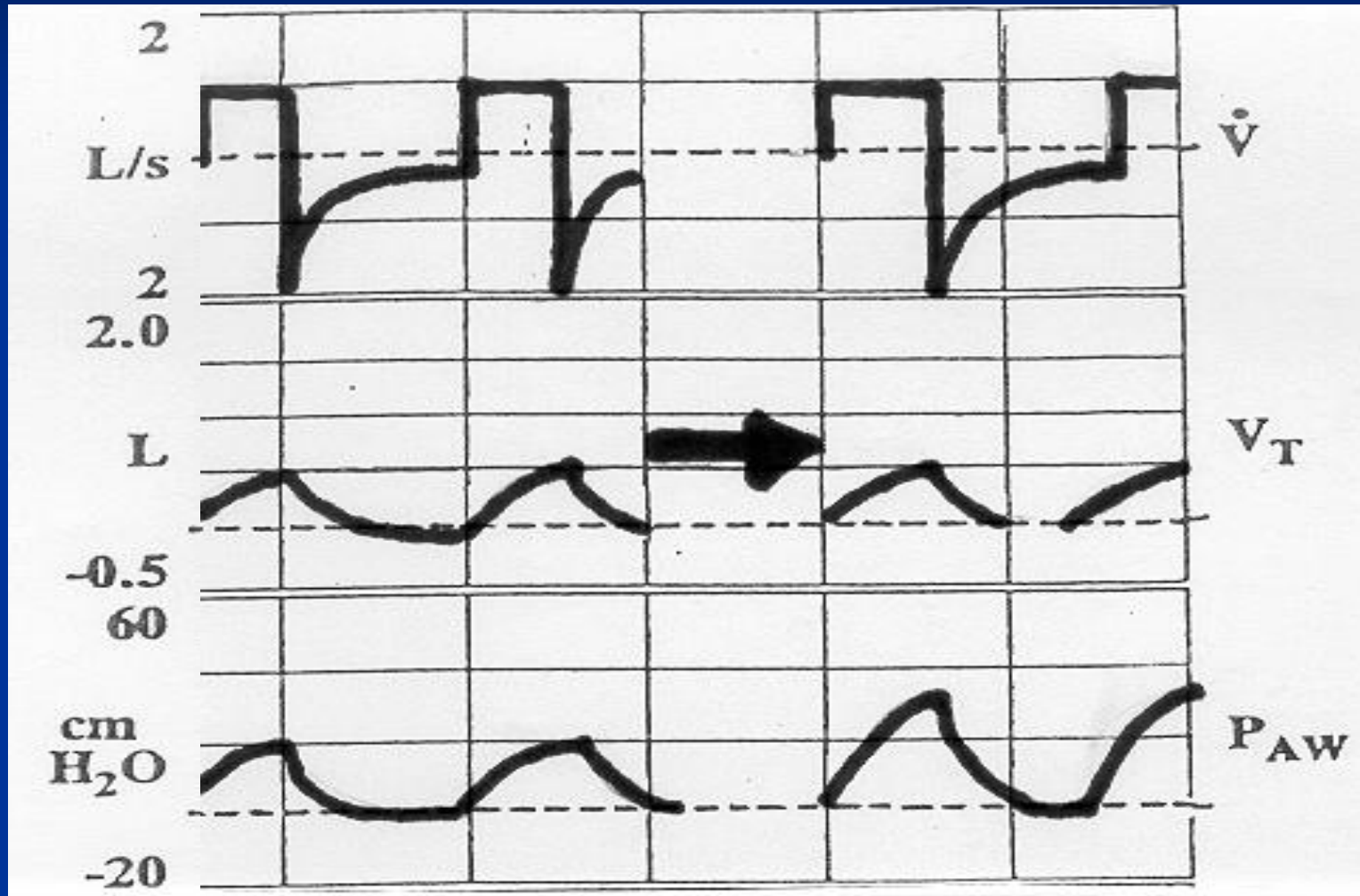
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Case 1:

A patient with severe COPD has been placed on a mechanical ventilator in volume assist control for respiratory support (initial delivered tidal volume 6 ml/kg, rate 30). Over the next several hours, however, her PCO₂ has climbed from 38 mmHg to 56 mmHg and her ventilator graphical display has changed. What is one thing to change that would help?

COPD with rising PCO_2



COPD with rising PCO_2

- A Increase rate
- B NMB
- C PACV
- D decrease rate
- E add PEEP

Case 2

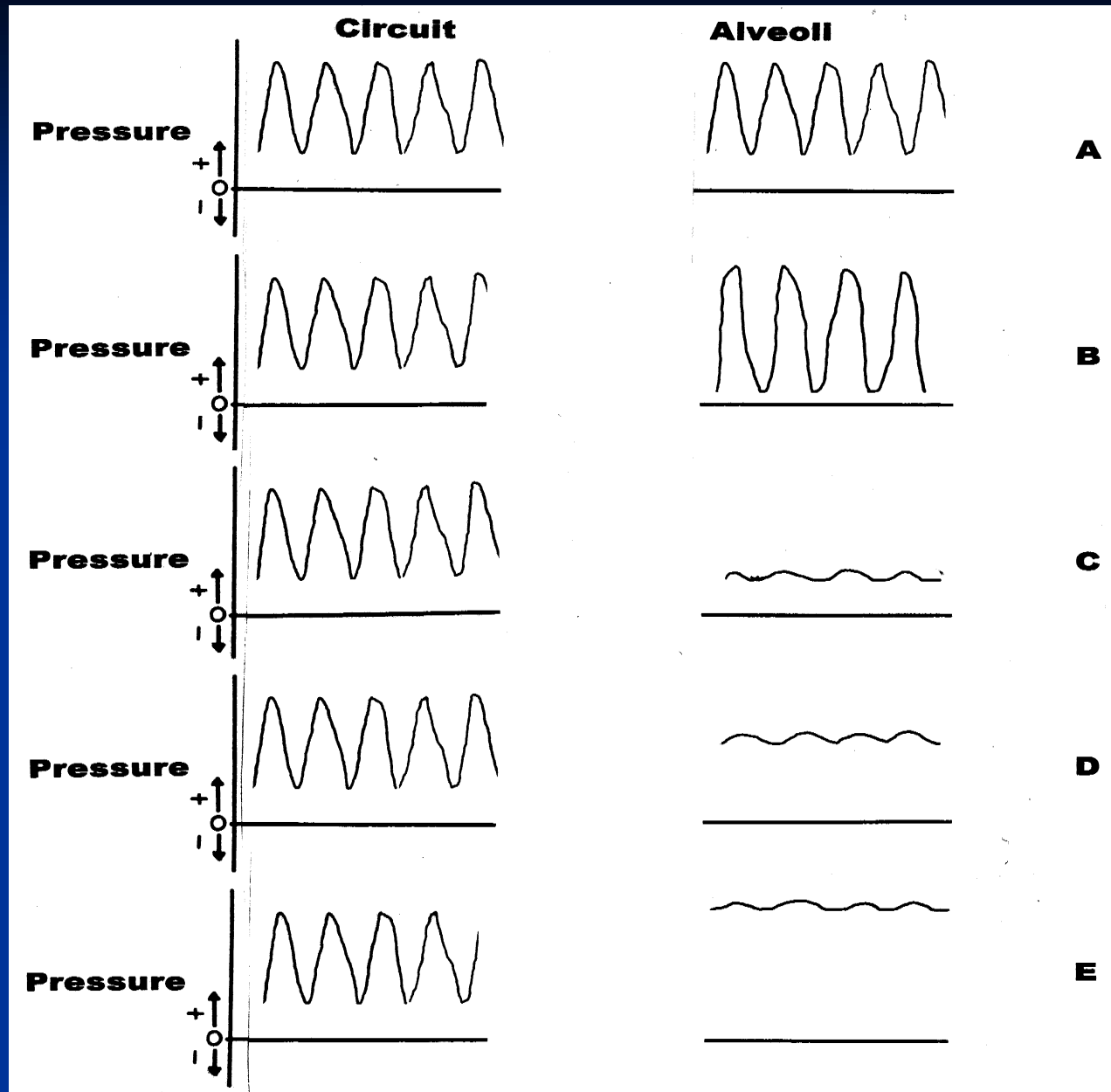
- A massively obese patient has undergone bariatric surgery. He is in the ICU requiring mechanical ventilatory support for an aspiration. His VT is 6ml/kg (IBW) but his P_{plat} is 37 cm H₂O. His PaCO₂ is 58 mmHg and the pH is 7.28. An esophageal balloon is placed to assess chest wall mechanics and the P_{es} is found to be 17 cm H₂O at end inspiration. What should be done with the VT setting?

Pplat 37, VT 6 ml/kg, Pes 17, pH 7.28

- A. VT should be reduced (reduce Pplat)
- B. VT should be maintained
- C. VT should be increased

Case 3

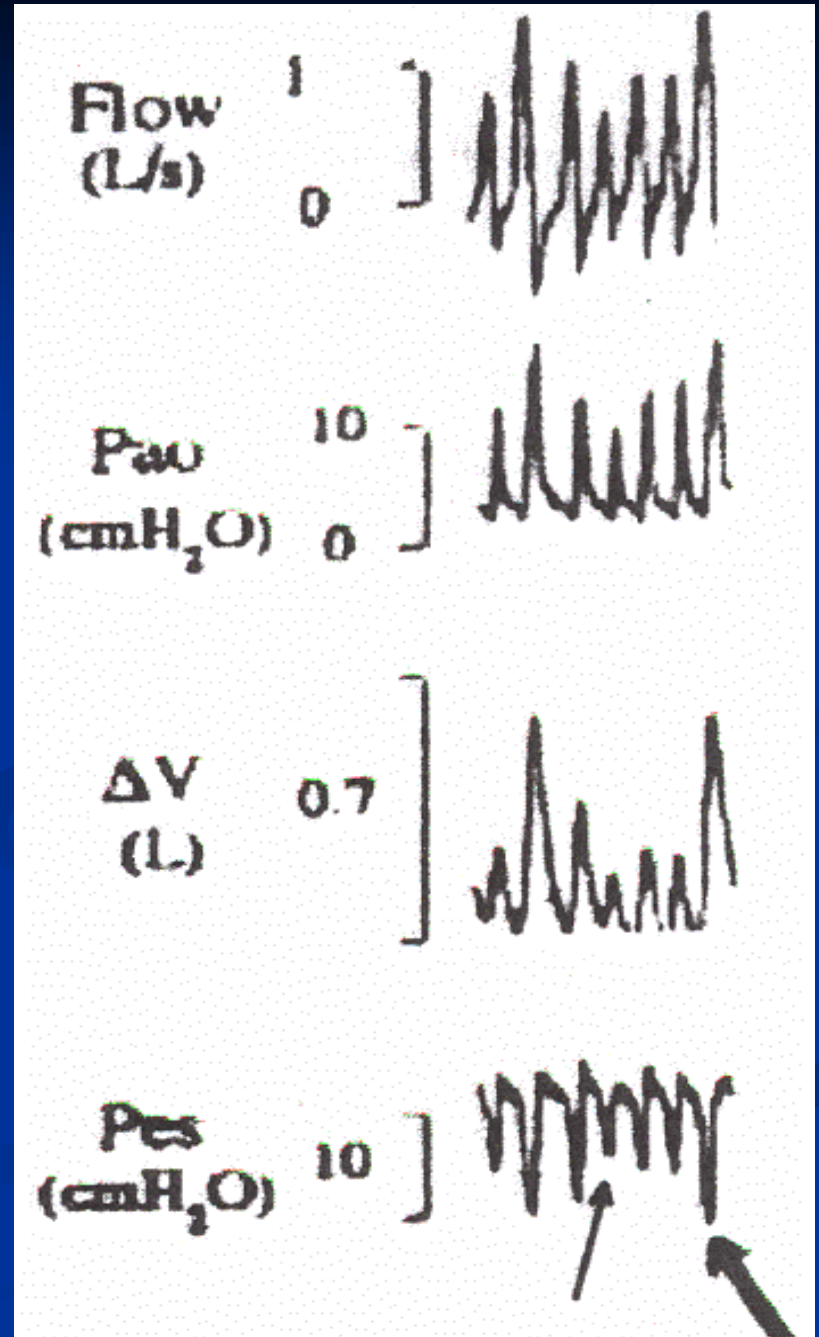
- A patient with ARDS is receiving high frequency ventilation. The relationship between airway (circuit) pressure and alveolar pressure is:



Case 4

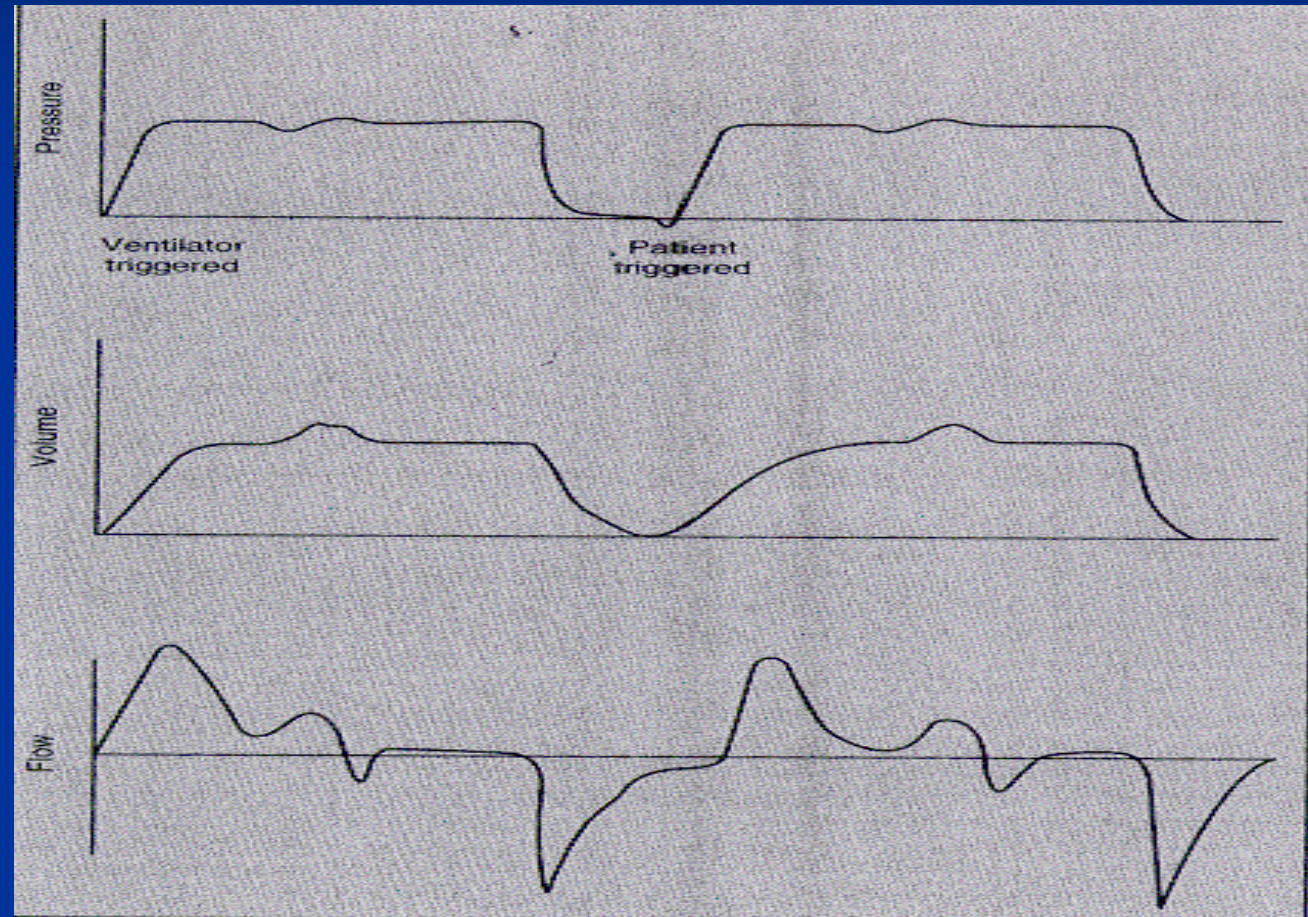
A patient is receiving the pictured mode of MV. The thin arrow represents a weak effort, the thick arrow represents a strong effort. What is this mode:

- A. Proportional assist (PAV)
- B. Volume support (VS)
- C. Volume assist control (VACV)
- D. Pressure support (PS)
- E. Airway pressure release ventilation (APRV)



Case 5: A patient with ARDS is being ventilated with the following mode - what is it?

- A PS
- B PCIRV
- C VACV
- D SIMV
- E APRV



P

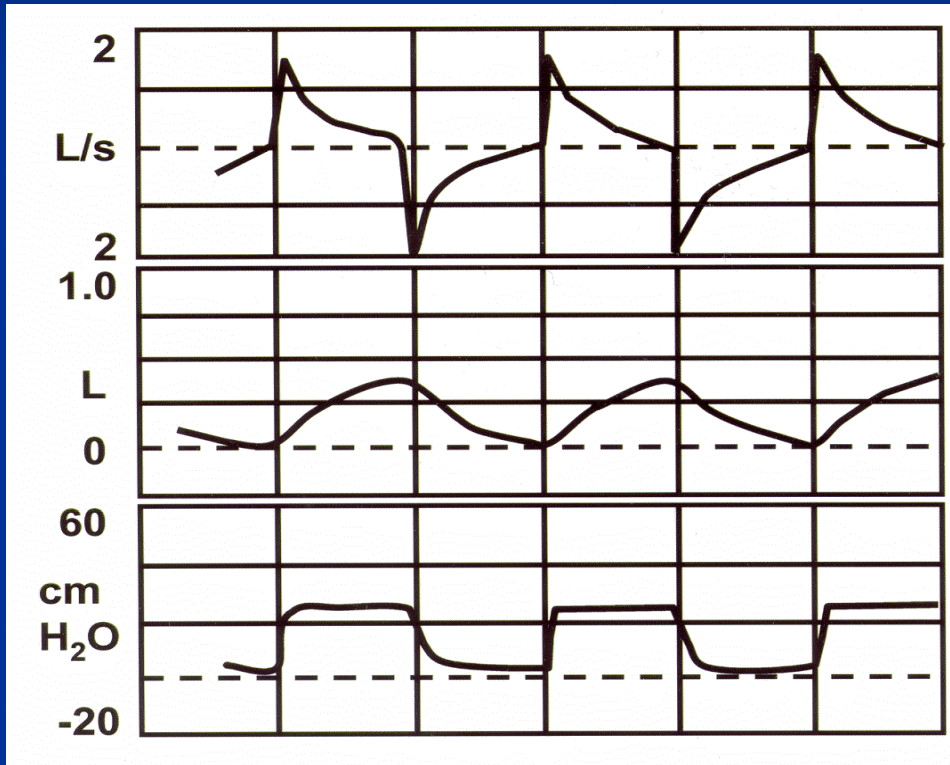
V

V'

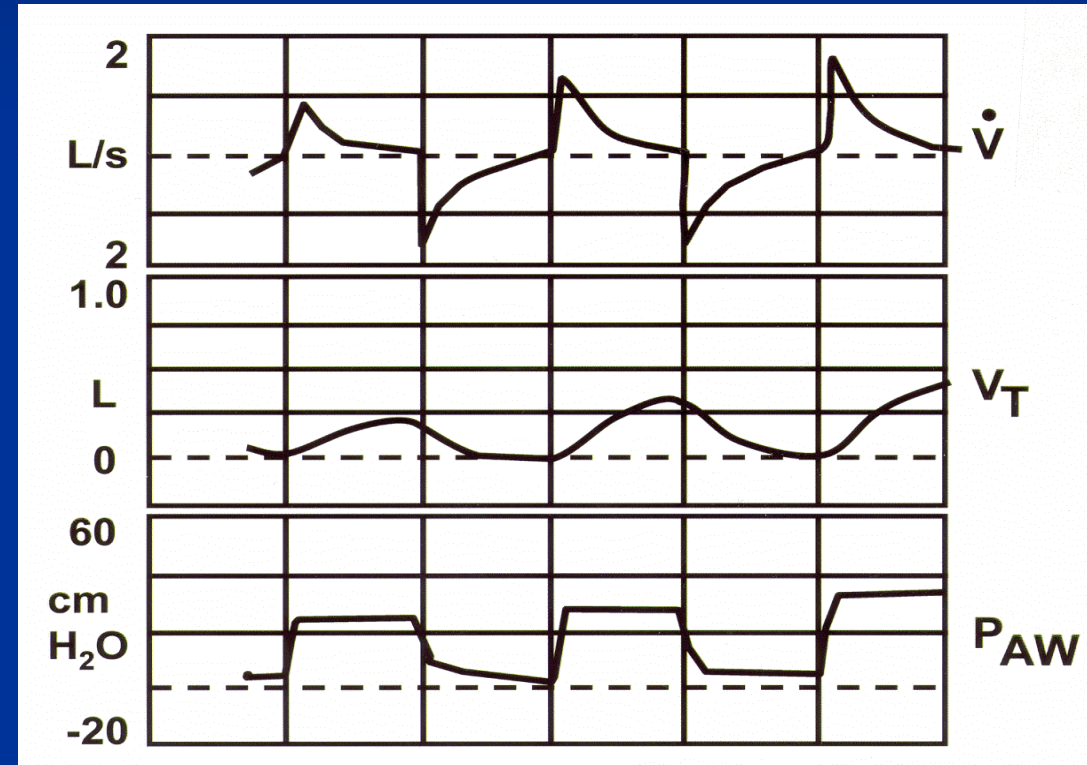
Time

Case 6

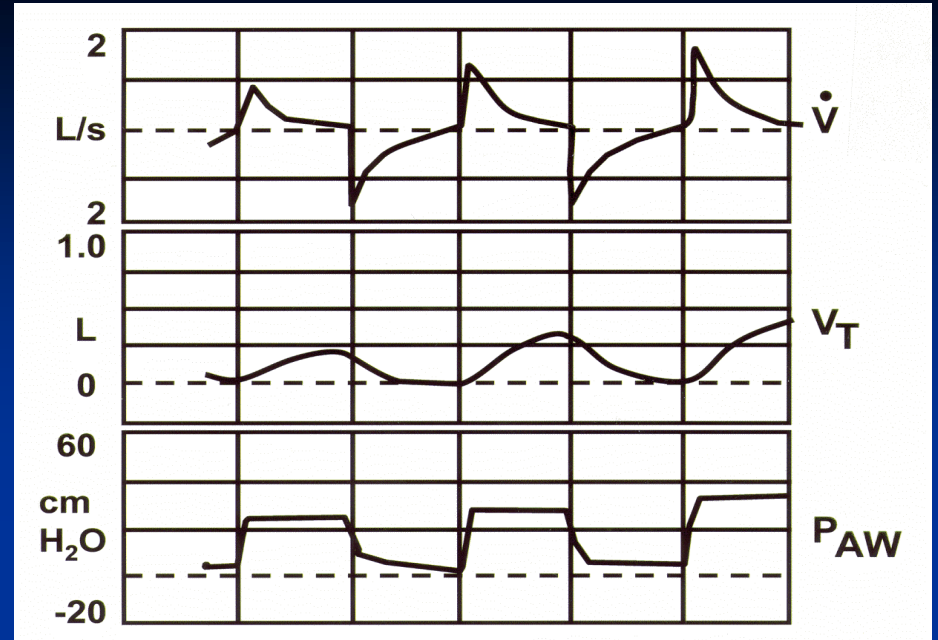
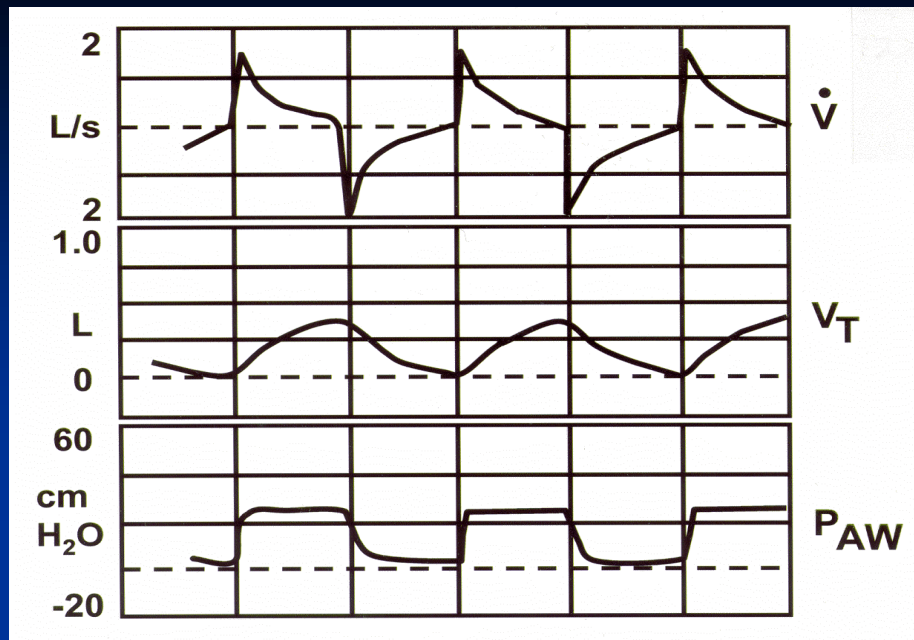
Compliance worsens between A and B – What mode behaves like this?



A



B



- A. Proportional assist
- B. SIMV
- C. Pressure support
- D. Pressure regulated volume control
- E. Volume support

Case 7: 78 yo recovering from sepsis/ARDS

- Gas exchange good on 5 cmH₂O PEEP and FiO₂ 0.4. Passes SBT with f/VT 40. Minimal secretions and good cough. Afebrile. However, responds only minimally to loud noises and sternal rub (GCS = 8). Sedation has been held since midnight and it is now 9 am. Would you extubate him now?
 - A. Yes
 - B. No

Case 8

A 44 yo woman with severe ARDS following chest trauma is receiving controlled mechanical ventilation with 6ml/kg tidal volume and a breathing frequency of 24 breaths/min. Her flow graphic shows that expiratory time is at the limit for preventing air trapping. Her FiO₂ is 0.5 and her PEEP setting is 12 cm H₂O. The resulting plateau pressure is 29 cm H₂O. On these settings, her arterial blood gas analysis shows: PCO₂ 66 mm Hg, pH 7.19, PO₂ 79 mm Hg. This respiratory acidosis:

- A. Should be corrected by increasing the tidal volume
- B. Should be corrected by increasing the frequency
- C. Should be corrected with bicarbonate infusion
- D. Should be tolerated

Case 9

In applying smaller tidal volumes during mechanical ventilation to afford lung protection in ARDS, assuring proper patient ventilator synchrony generally requires:

- A. More sedation
- B. Sodium bicarbonate to treat any respiratory acidosis
- C. Higher PEEP requirements
- D. No specific therapies beyond good respiratory care

Case 10

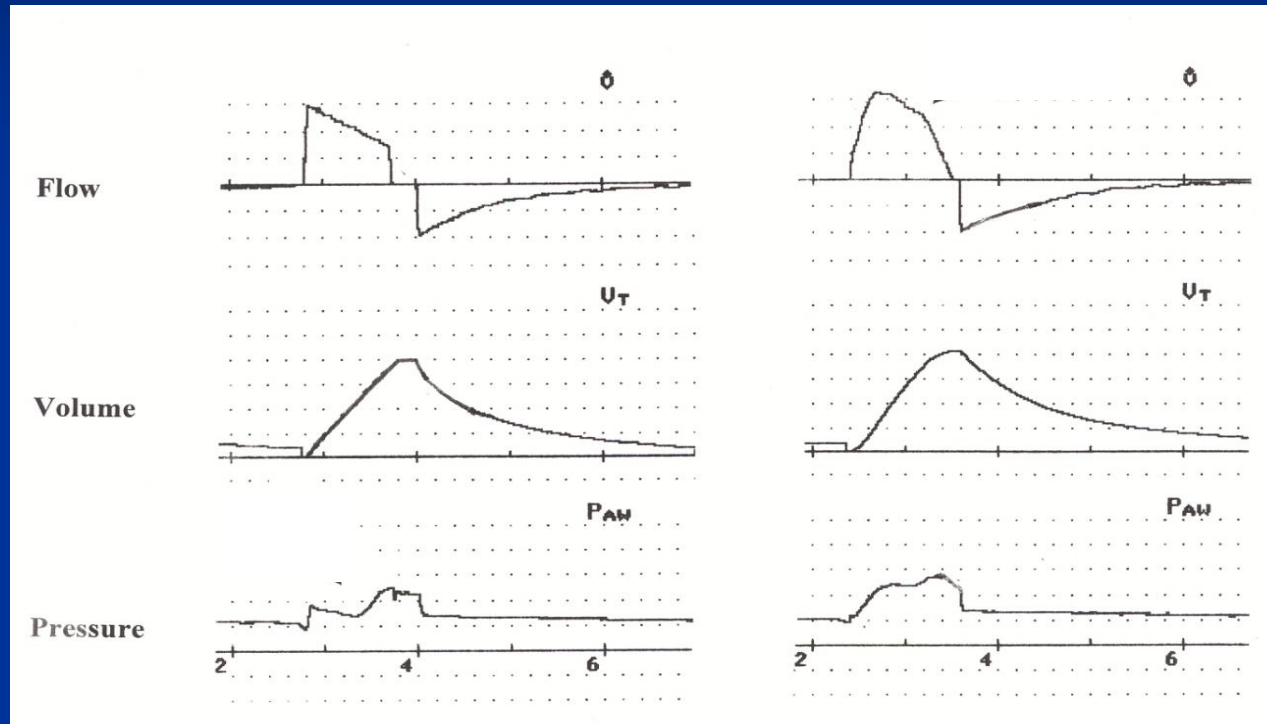
A patient with ARDS has the chest computerized tomographic scan depicted. Compared to the lower half of the lungs (dependent regions), the upper half of the lungs (non-dependent regions) during a positive pressure breath will:



- A. Have a higher regional inspiratory plateau pressure (P_{plat}) but comparable regional tidal volume
- B. Have a lower regional P_{plat} but comparable regional tidal volume
- C. Have a comparable P_{plat} but higher regional tidal volume
- D. Have comparable regional P_{plat} and regional tidal volume

Case 11

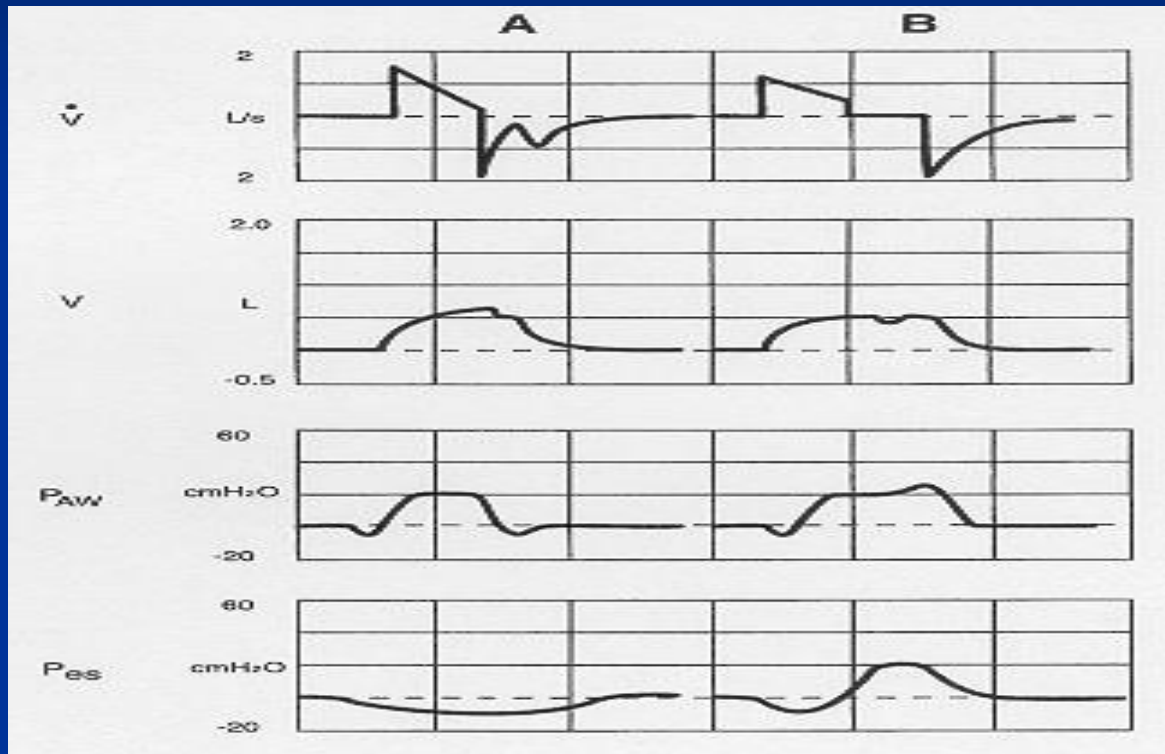
A patient has the ventilator adjusted from the left to the right panel to improve comfort. What is the adjustment and was it successful?



- A. Change to volume assist control with improved comfort
- B. Change to pressure support with improved comfort
- C. Change to volume assist control with worsened comfort
- D. Change to pressure support with worsened comfort

Case 12

The breath cycling in these two breaths are:



- A. Both appropriate for synchrony
- B. A is too short, B is too long
- C. A is too long, B is too short
- D. A and B are both too short

Case 13

What adjustment to these breaths is occurring?



- A. Change in pressure support level
- B. Change in pressure support flow cycling criteria
- C. Change in rise time (slope) of pressure support
- D. Change in volume target

Life Threatening Bronchospasm

Neil MacIntyre MD

Duke University Medical Center

Durham NC

Life Threatening Asthma

- Definitions and incidence
- Pathophysiology and clinical picture
- Pharmacologic strategies
- Mechanical ventilation issues
- Outcome

Definition of LTA

- One or more of the following:
 - Respiratory arrest
 - Need for MV
 - Respiratory acidosis $\text{PCO}_2 > 50/\text{pH} < 7.3$
 - LOC
 - Death

Question

- What is the yearly mortality from asthma in the US:
 - A. <1000
 - B. 4000-6000
 - C. 10000-12000
 - D. 20000-25000

Incidence of LTA

- In the United States:
 - 1.5 million ED visits/year for asthma
 - 20% of these visits require hospitalization (LTA)
 - 4% of admissions require ICU care
 - Asthma mortality 1.5/100,000 population (4200/yr)
 - 3.7/100,000 in Afr-Amer, 0.3/100,000 in age < 18
- ED and hospitalized asthma care accounts for 50% of total asthma costs

Life Threatening Asthma

- Definitions and incidence
- Pathophysiology and clinical picture
- Pharmacologic strategies
- Mechanical ventilation issues
- Outcome

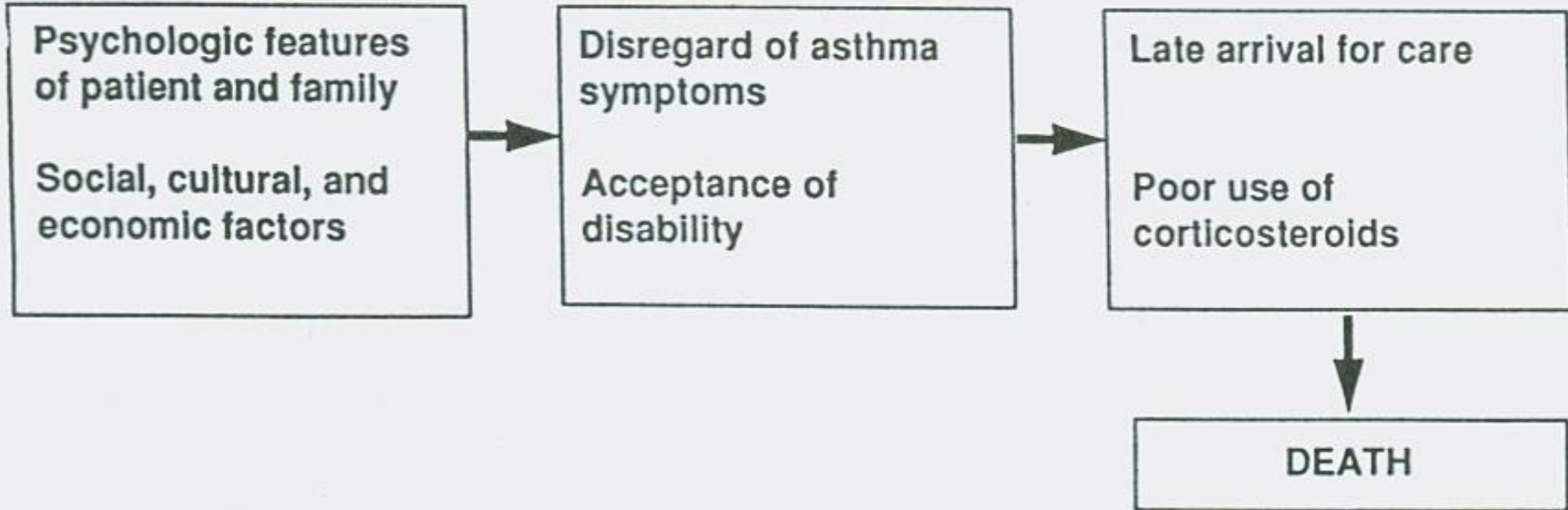
Risk factors for LTA

- Strongest – previous LTA occurrence or hospitalization
- Other important factors:
 - Access/compliance issues
 - Blunted hypoxic drive/sense of dyspnea
 - Large diurnal PF variability
 - Drugs – NSAID, beta blockers
 - Allergens
 - Psychiatric
- Controversial factors: Methacholine sensitivity, beta agonist overuse (most are undertreated!)

Clinical presentation

- Two variants:
 - Rapid onset: <2 (?6)hrs
 - Slower onset: >2 (?6) hrs
- Rapid is reported from 8-58% of LTA
 - Using the 2 hour definition, closer to 20 %

Type 1: Slow onset, late arrival



Type 2: Sudden onset







Important clinical features of LTA

- Paradoxical pulse > 25
- Silent chest/feeble respirations
- Bradycardia/hypotension
- Cyanosis
- Lactic acidosis
- Confusion/coma
- Pneumothorax/pneumomediastinum

Life Threatening Asthma

- Definitions and incidence
- Pathophysiology and clinical picture
- Pharmacologic strategies
- Mechanical ventilation issues
- Outcome

Pharmacotherapy in LTA

- Bronchodilators
 - Beta agonists, anti-cholinergics, xanthines
- Corticosteroids
- Oxygen
- Magnesium sulfate
- Leukotriene antagonists

Bronchodilators in LTA

- Controversies
 - IV vs inhaled
 - MDI vs nebulizer
 - Dosing

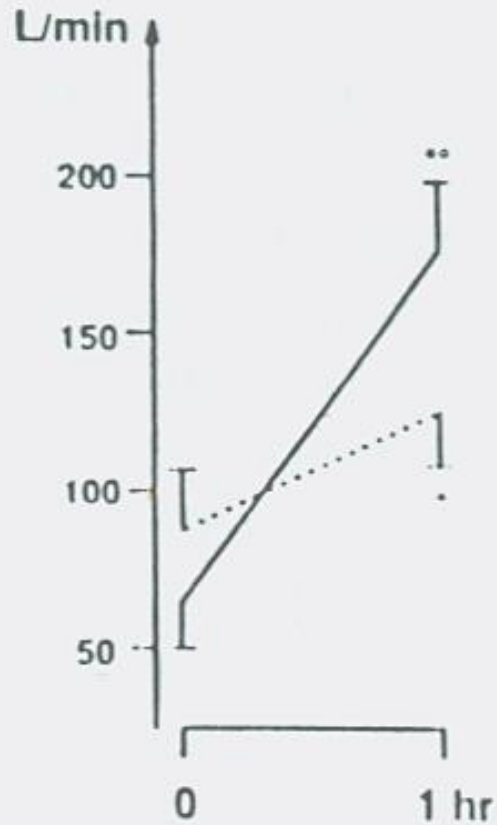
Question:

- Intravenous beta agonists are more effective than properly aerosolized beta agonists:
 - A. True
 - B. False

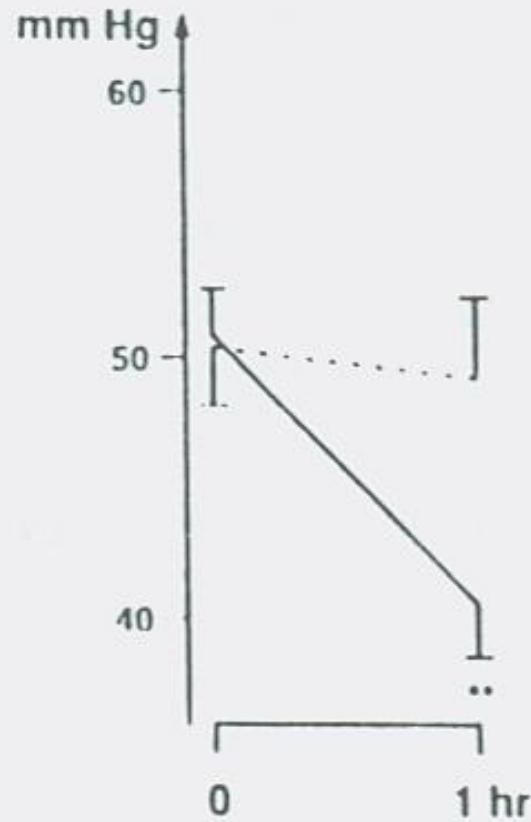
Bronchodilators in LTA

- Controversies
 - IV vs inhaled
 - Inhaled may be faster with fewer side effects
 - MDI vs nebulizer
 - Dosing

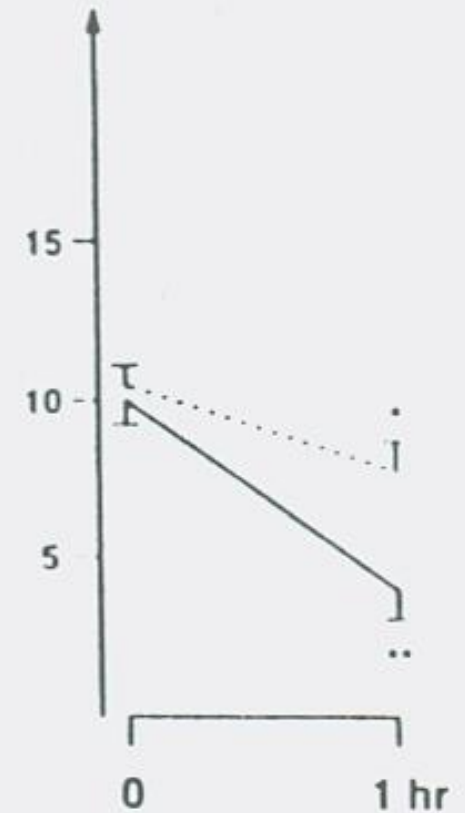
PEF



PaCO2



Clinical Index



Time

Inhaled (solid) vs IV (dashed) beta agonist

Sheffer, Fatal Asthma, Marcel Decker 1998

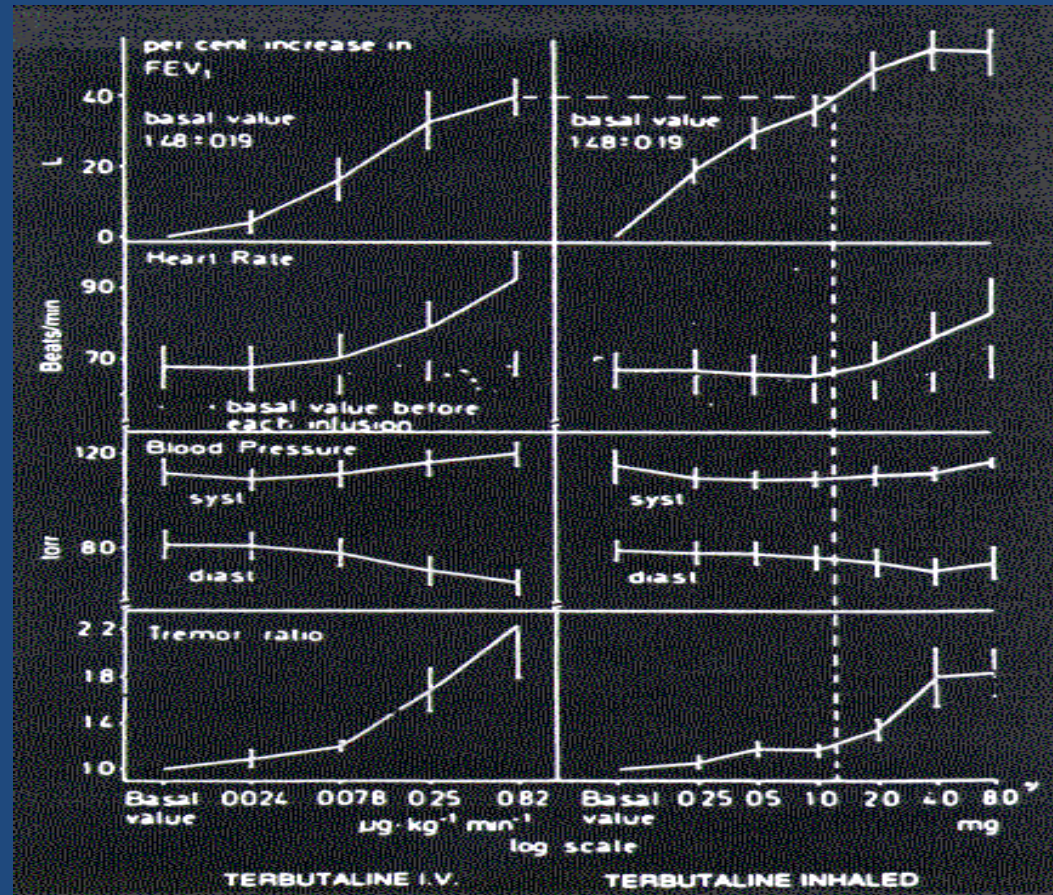
IV vs inhaled beta agonist

FEV₁

HR

BP

Tremor



IV

Aerosol

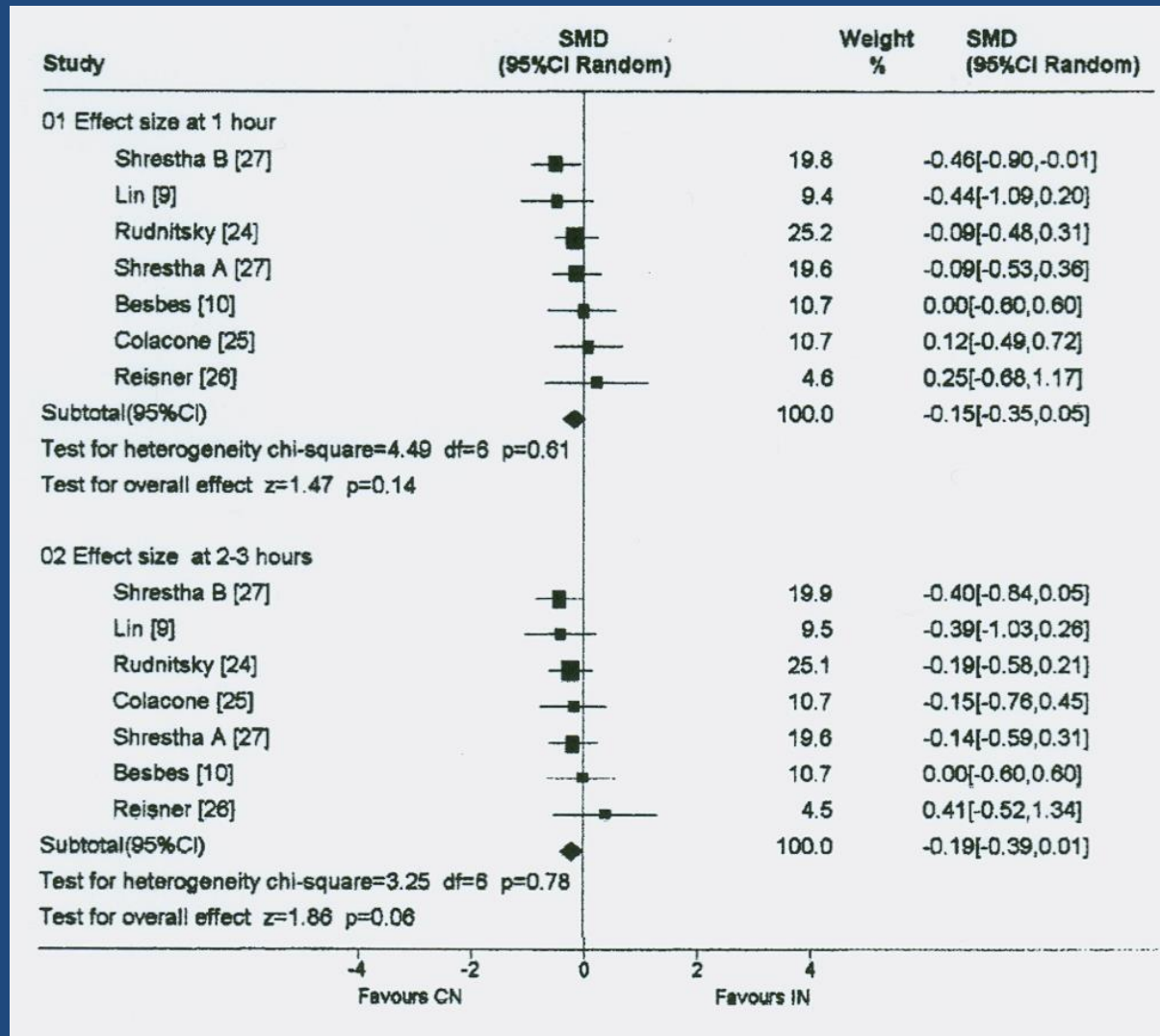
Bronchodilators in LTA

- Controversies
 - IV vs inhaled
 - MDI vs nebulizer
 - Equally effective *IF* patient can work with MDI/spacer
 - High volume nebs can deliver higher doses with tidal breathing
 - Dosing

Bronchodilators in LTA

- Controversies
 - IV vs inhaled
 - MDI vs nebulizer
 - Dosing
 - High doses – push to effect – continuous?
 - Best responses in those with smooth muscle spasm

Continuous vs Intermittent Albuterol



*Chest 2002;
122: 160*

Pharmacotherapy in LTA

- Bronchodilators
 - Beta agonists, anti-cholinergics, xanthines
- Corticosteroids
- Oxygen
- Magnesium sulfate
- Leukotriene antagonists

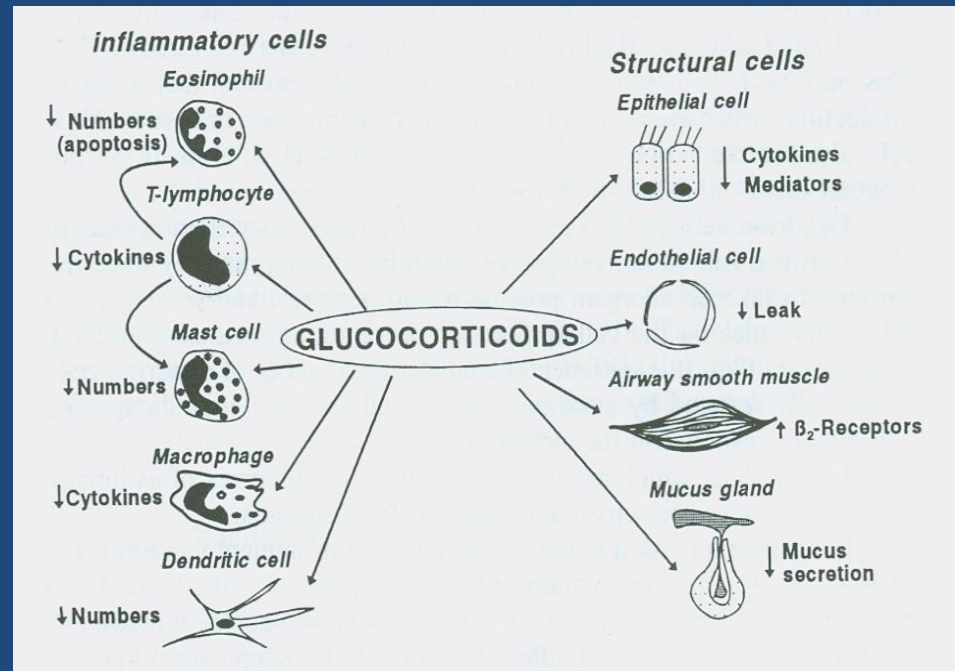
Additional BD in LTA

- Anticholinergics (up to 500 ug q 20min in neb)
 - Added benefit to high dose albuterol in terms of:
 - Reduced hospitalization rates (38% vs 57%)
 - Improved PEFR
 - Reduced costs
- Theophylline
 - Adds considerable toxicity in setting of high beta agonist use – reserve for use only in the most refractory patients

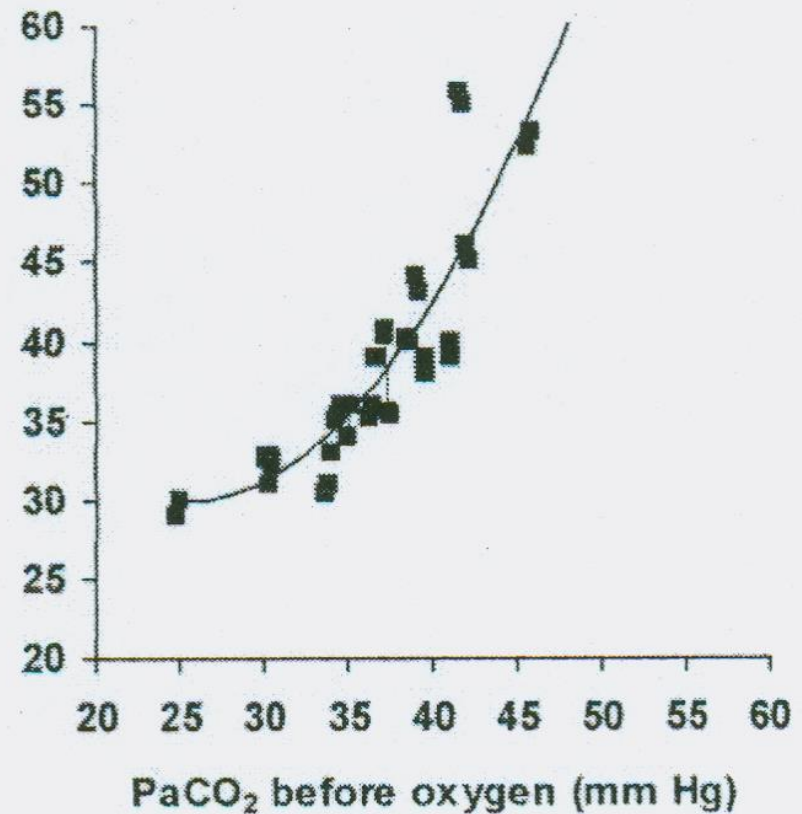
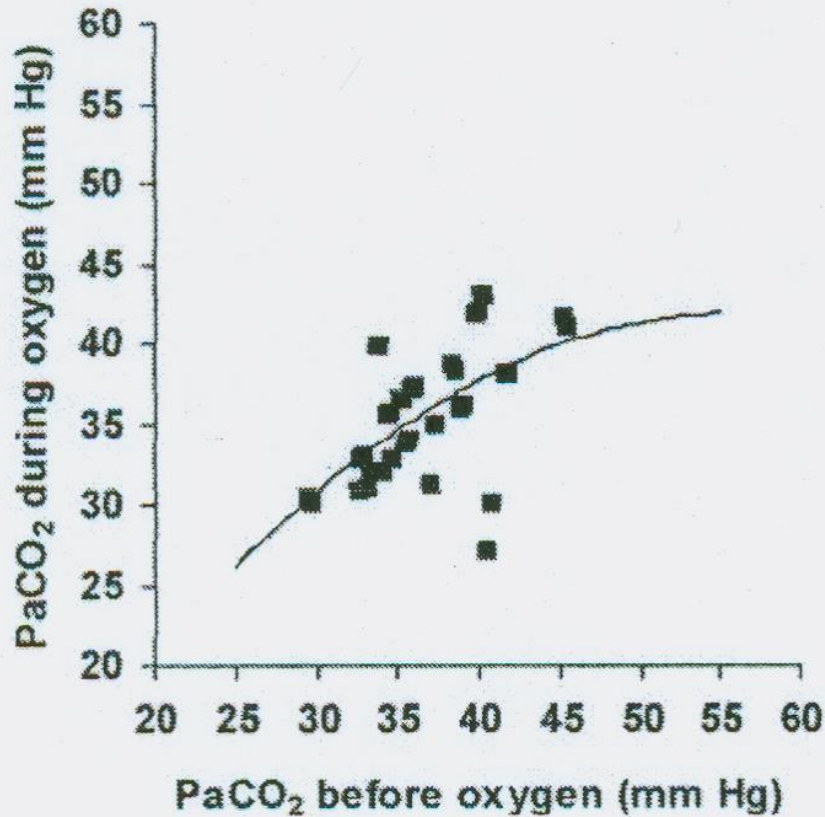
Corticosteroids

Steroids: Cochrane Review

- 12 RCTs favor steroids - esp in severe.
- Oral = IV, super high doses not needed
- Systemic effect may take hours - Inhaled (if pt can do MDI) may produce faster effects
 - Vasoconstriction
 - Beta agonist sensitivity



Oxygen titrated to SpO2



SpO₂ target 88-92

SpO₂ target > 95

Should be humidified

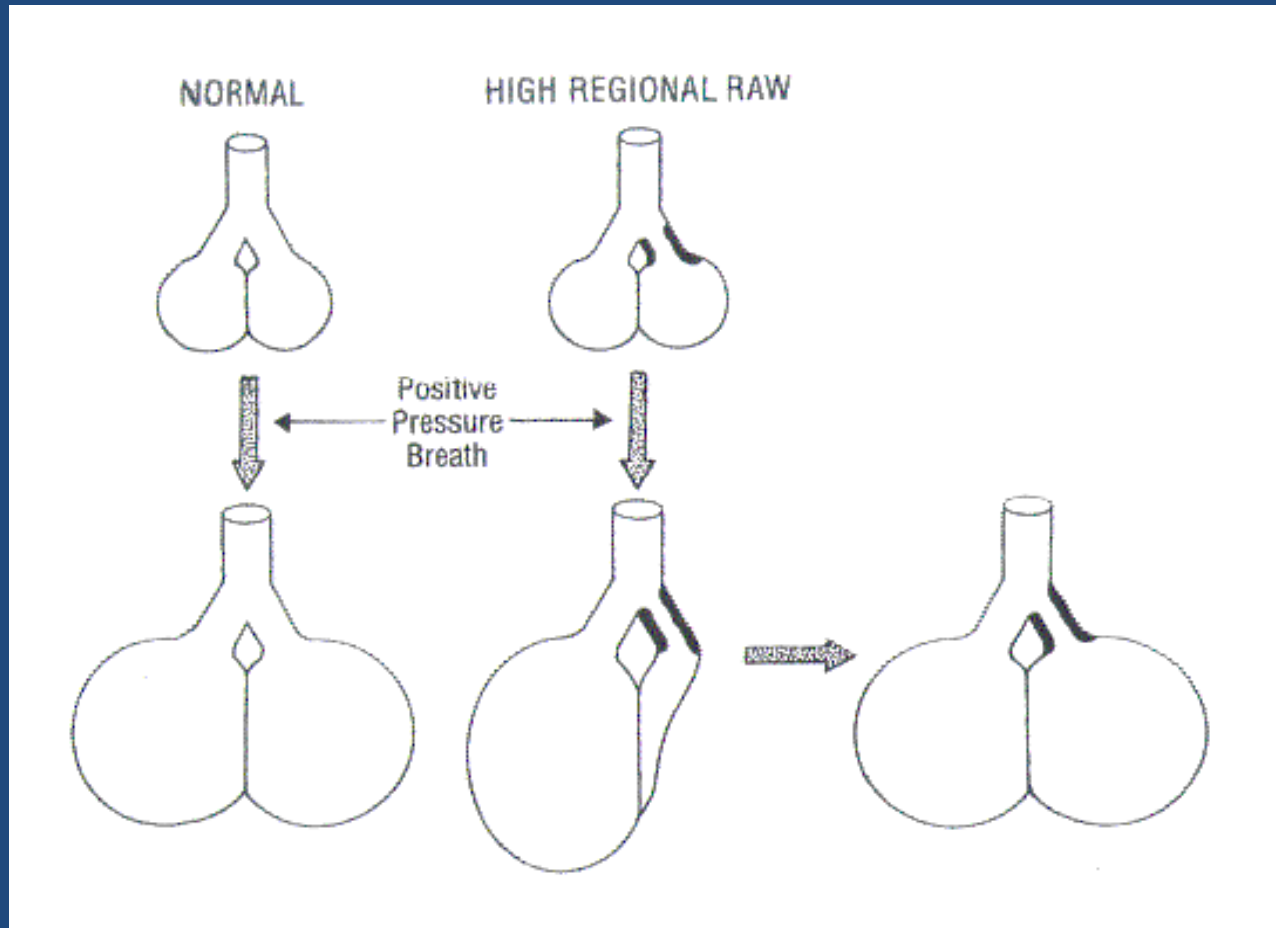
Others

- MgSO₄ –
 - Blocks muscle contraction
 - 7 RCTs in Cochrane - 665 pts
 - all on steroids/nebs
 - benefits in severe, not in general (reduced admissions) –
 - 2 gm over 20 minutes
 - Should be used as adjunct only (Chest 2002;122:489)
- Leukotriene antagonist–
 - Possible adjunctive therapy (IV improved PFT, dyspnea)
AJRCCM 2003;166:528

Life Threatening Asthma

- Definitions and incidence
- Pathophysiology and clinical picture
- Pharmacologic strategies
- Mechanical ventilation issues
- Outcome

Avoiding overdistention



Considerations in providing invasive PPV

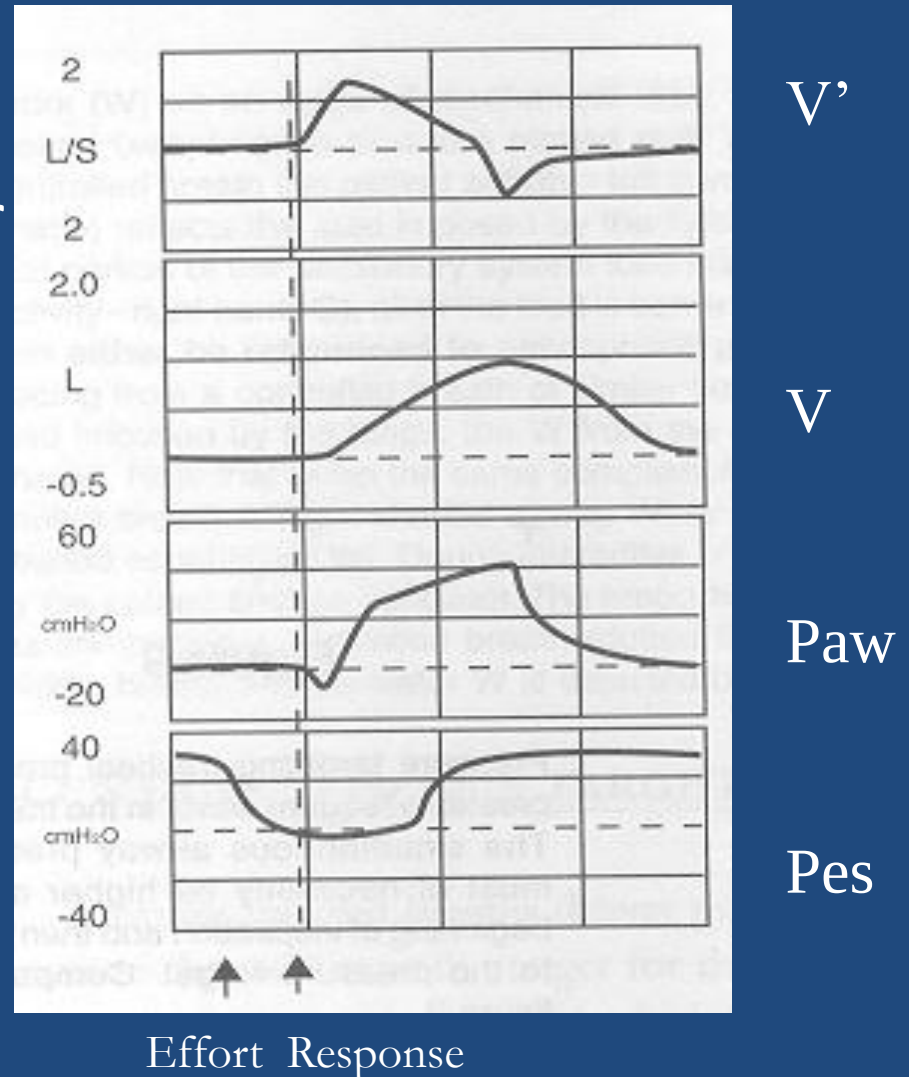
- Regional overdistention injury applies to asthma patients just as it does to ARDS patients
- Therefore:
 - strategies should be similar to protecting healthy lung units in other forms of respiratory failure
 - permissive hypercapnia is a reasonable tradeoff
 - healthier regions exposed to higher than P_{plat} (near P_{peak}) at beginning of breath
- Issue of PEEPi

PEEPi

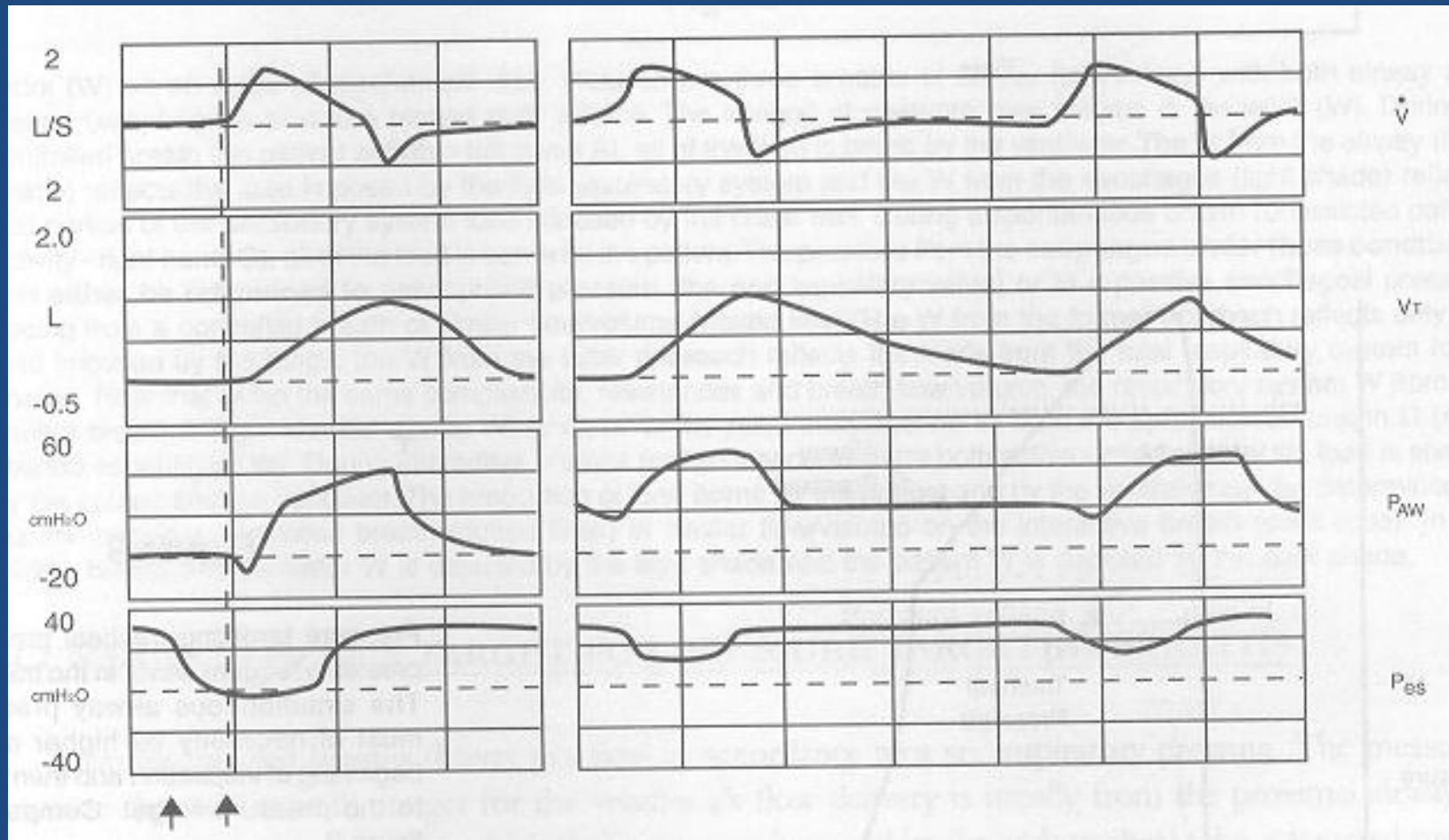
- Effects:
 - Raises end insp P for a constant VT
 - Triggering load
- Determinants:
 - MV (f and VT effects equal)
 - I:E
 - R x C (incl airway collapse)
- To treat, must reverse one of the three determinants

Question: Trigger problems in OAD

- A sedate
- B switch to flow trigger
- C PEEP 5
- D PEEP 20
- E switch to SIMV



After 20 cm H₂O PEEP



Note: Effort-response delay reduced while baseline P_{es} and Peak airway pressures have changed little

Heliox

(thru mask or vent)

- Reduces density to reduce flow related (ie peak-plateau) pressures
- Can reduce plateau pressure by improving emptying (ie reduce PEEPi) - may also improve breath triggering
- ? Augment aerosol delivery (NOT as drive gas)
- May affect ventilator flow measurements

Heliox lowers PEEPi

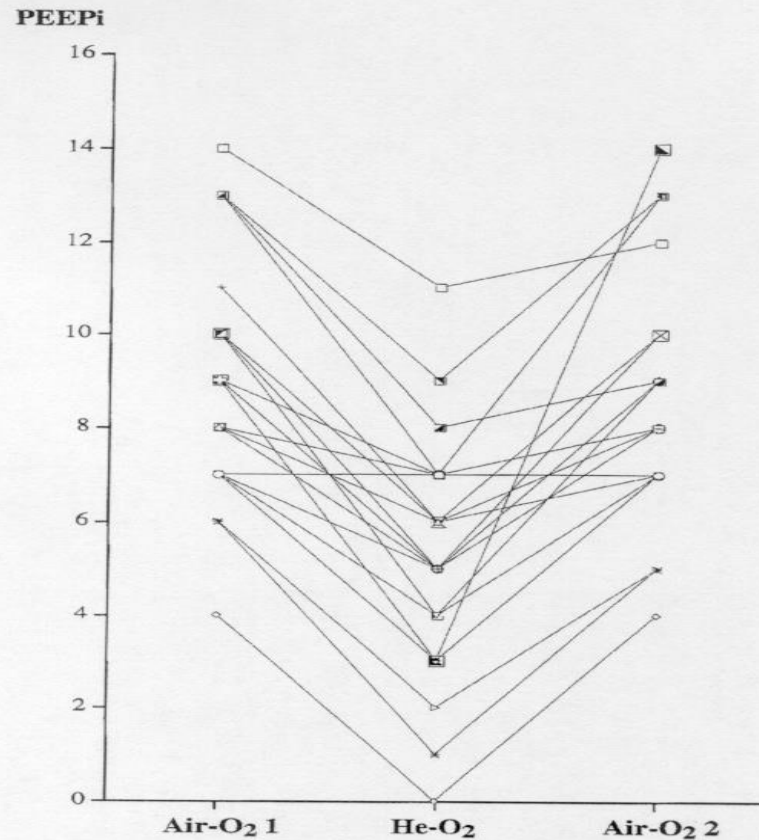
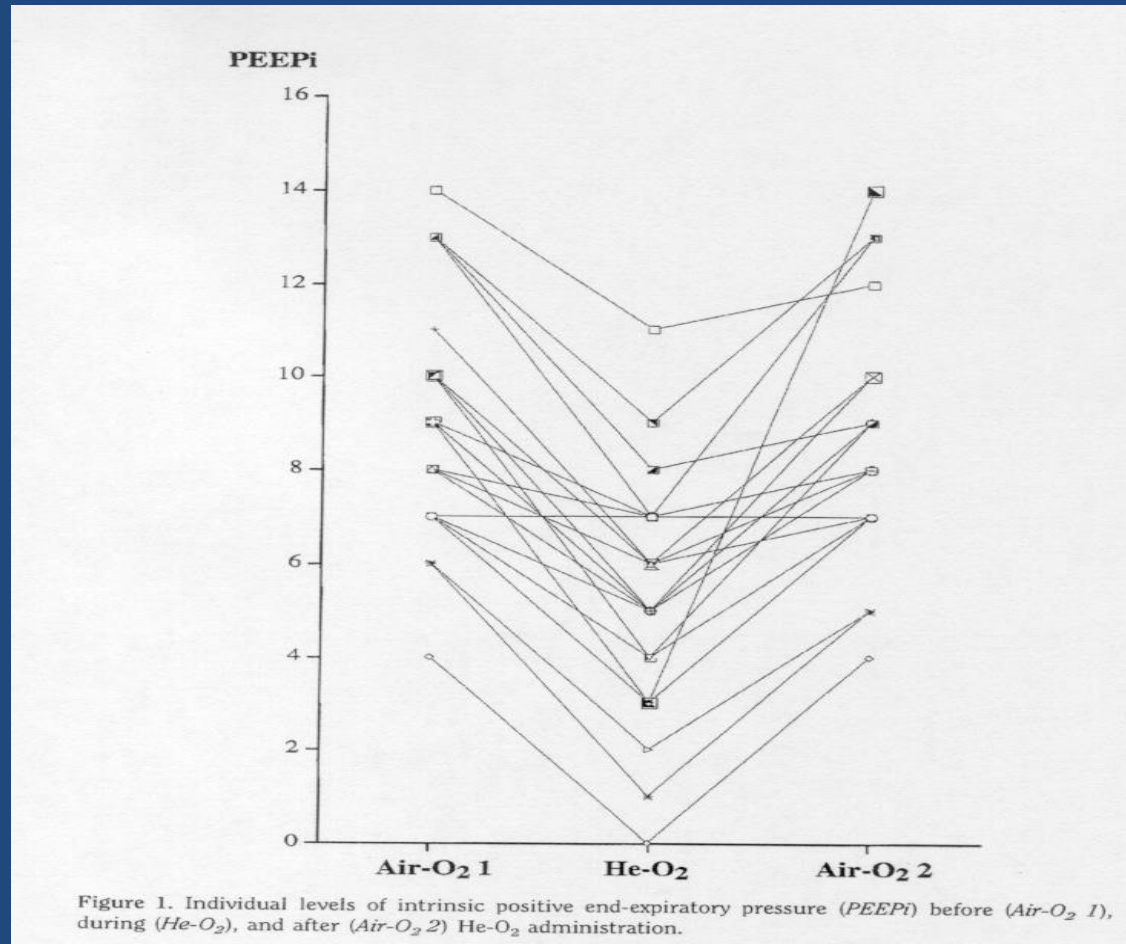


Figure 1. Individual levels of intrinsic positive end-expiratory pressure (PEEPi) before (Air-O₂ 1), during (He-O₂), and after (Air-O₂ 2) He-O₂ administration.

Heliox lowers PEEPi



Note: Heliox improves mechanics, stretch – NOT underlying disease process. Difficult to show outcome benefits

Unclear role in the mechanically ventilated patient

- General anesthesia
- Lavage
- Surfactant

Life Threatening Asthma

- Definitions and incidence
- Pathophysiology and clinical picture
- Pharmacologic strategies
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- Outcome

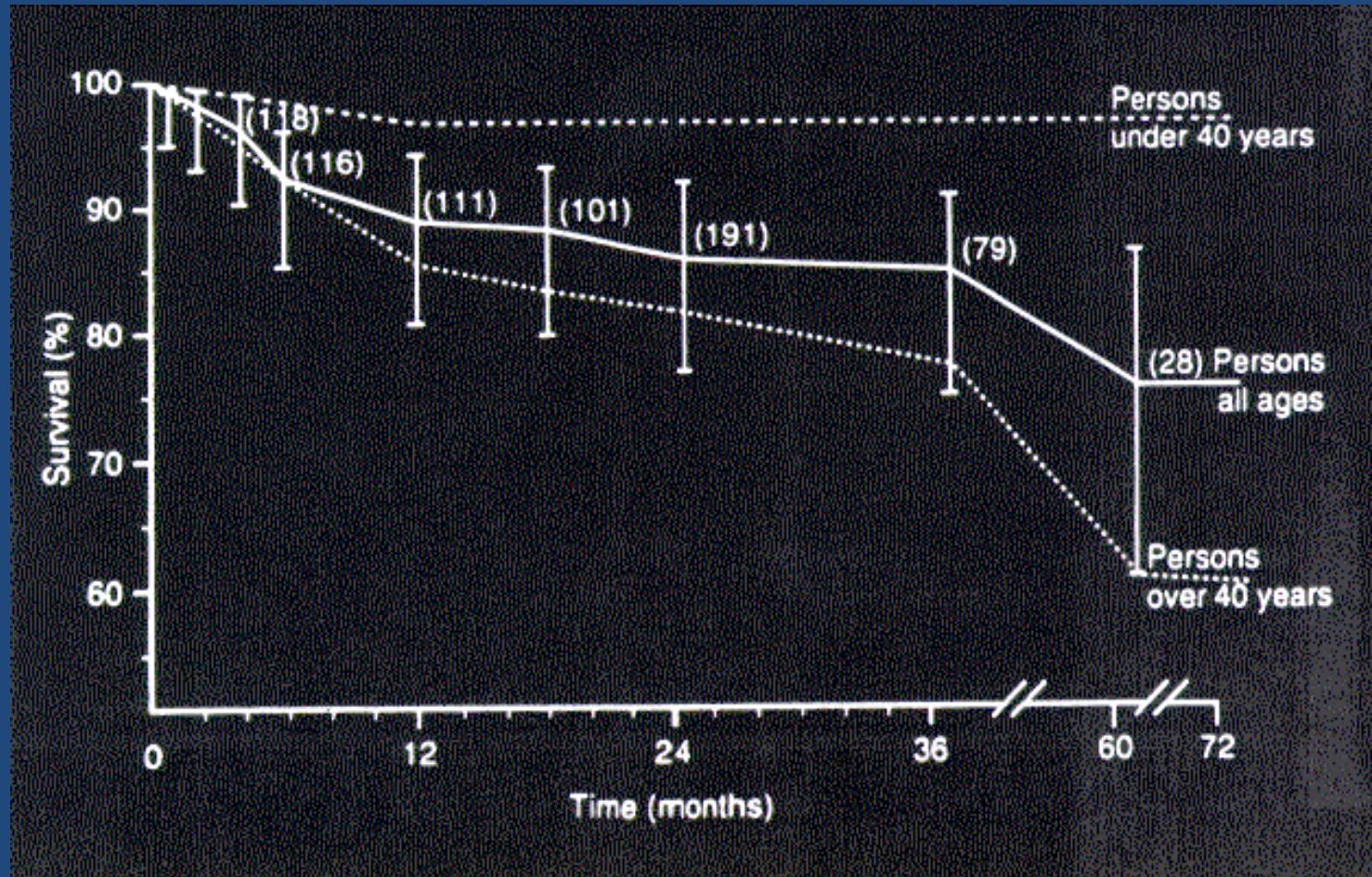
Short term outcomes in LTA

	Rapid n=45	Slow n=175
Steroid requirements	263 mg*	194 mg*
Days in hospital	8*	9.5*
Days in ICU	1	2
Hours of MV	13*	28*
Complications	22	31
Neuro sequelae	2.2	1.7
Death**	2.2	5.7

*P <0.05

Eur Resp J 2002;19:846

Long term outcome of patients intubated for asthma

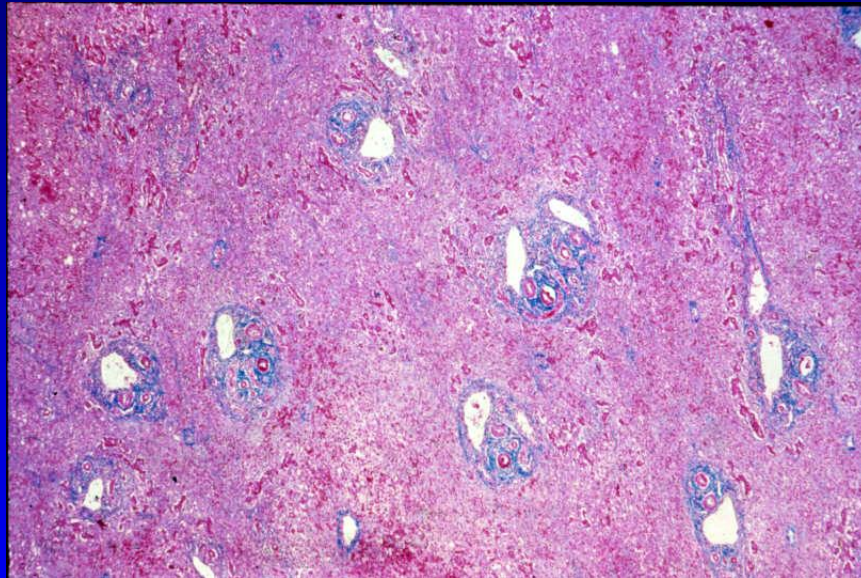


Life Threatening Asthma

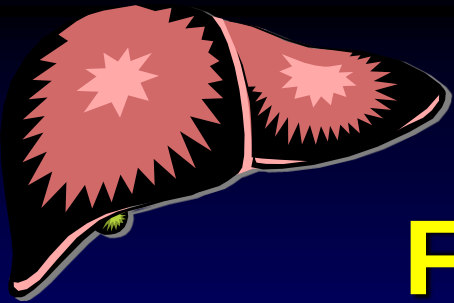
- Definitions and incidence
- Pathophysiology and clinical picture
- Pharmacologic strategies
- Mechanical ventilation issues
- Outcome

Fulminant Hepatic Failure

Current and Emerging Therapies



Robert J. Fontana, MD
University of Michigan Medical School



Fulminant Hepatic Failure

- Etiology and prognosis
 - Acetaminophen overdose
 - NAC for non-APAP ALF
- Cerebral edema
 - ICP monitoring
 - Medical therapy
- Liver transplantation

ALF overview

- **ALF is an uncommon but dramatic illness**
 - **DEFN:** Onset of coagulopathy (INR > 1.5) and encephalopathy within 8 (to 26) weeks in a patient without prior liver disease
 - **Exclude:** Alcoholic hepatitis, HBV reactivation, sepsis
- **Deterioration can be rapid & unpredictable**
 - Cerebral edema, infection leading cause of death
 - 30-40% spontaneous survival with ICU care
- **Liver transplantation → 75% 1 yr survival**

Evidence based management of ALF

- Rare clinical entity
 - 1 to 10 per 100,000 / yr
 - 2,800 cases/yr in US
 - Few RCT

+ Benefit	No benefit
NAC for ACM & non-ACM	Steroids in non-ACM
H ₂ blocker	Enteral abx
CVVHD	Charcoal hemoperfusion
Mannitol	Bioartificial liver Albumin dialysis

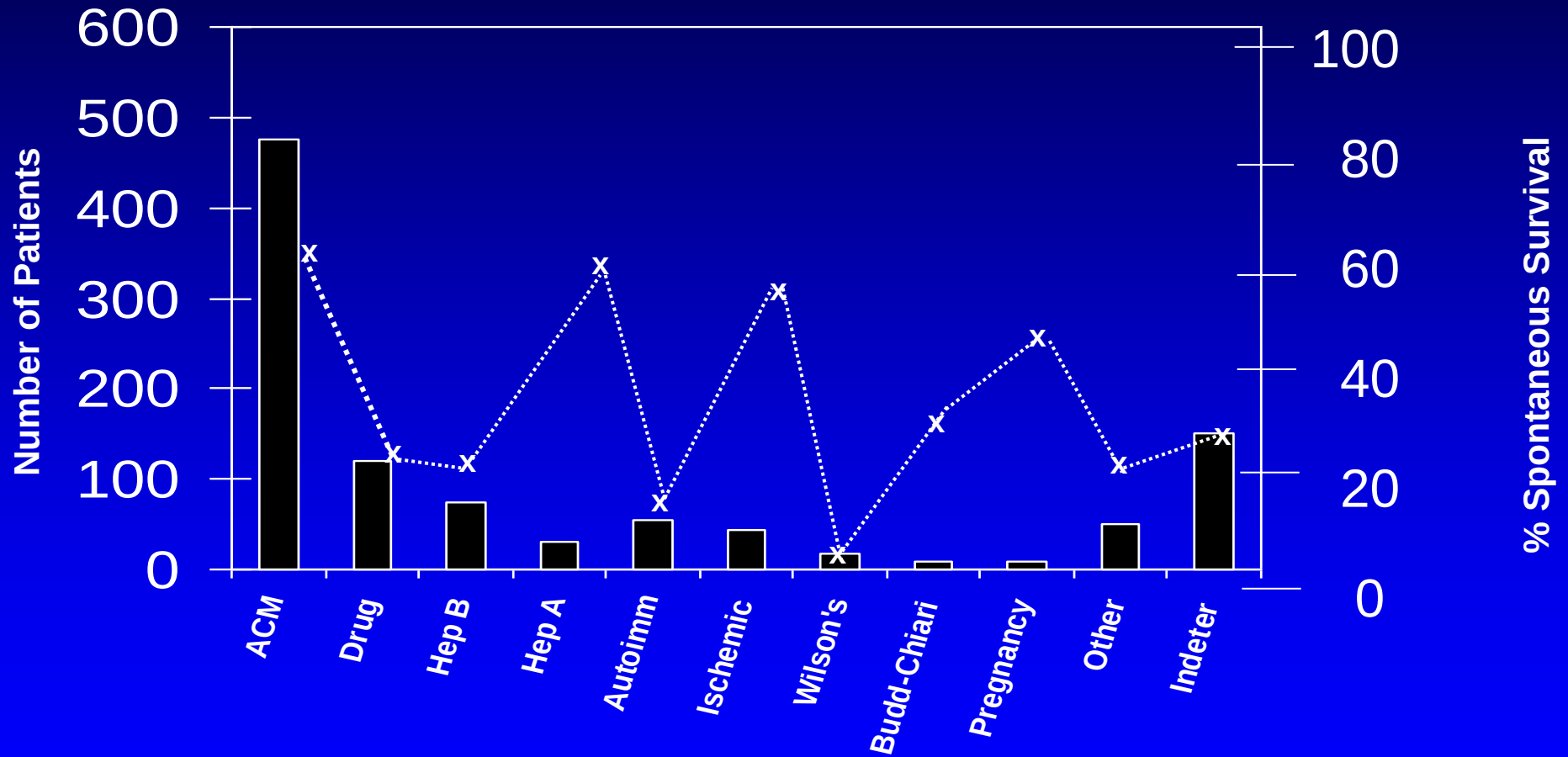
Question #1

- The leading cause of acute liver failure in the US is:
 - A. Acetaminophen overdose
 - B. Ischemic hepatitis
 - C. Hepatitis A
 - D. Hepatitis B

Step 1: Etiologic Screen for FHF

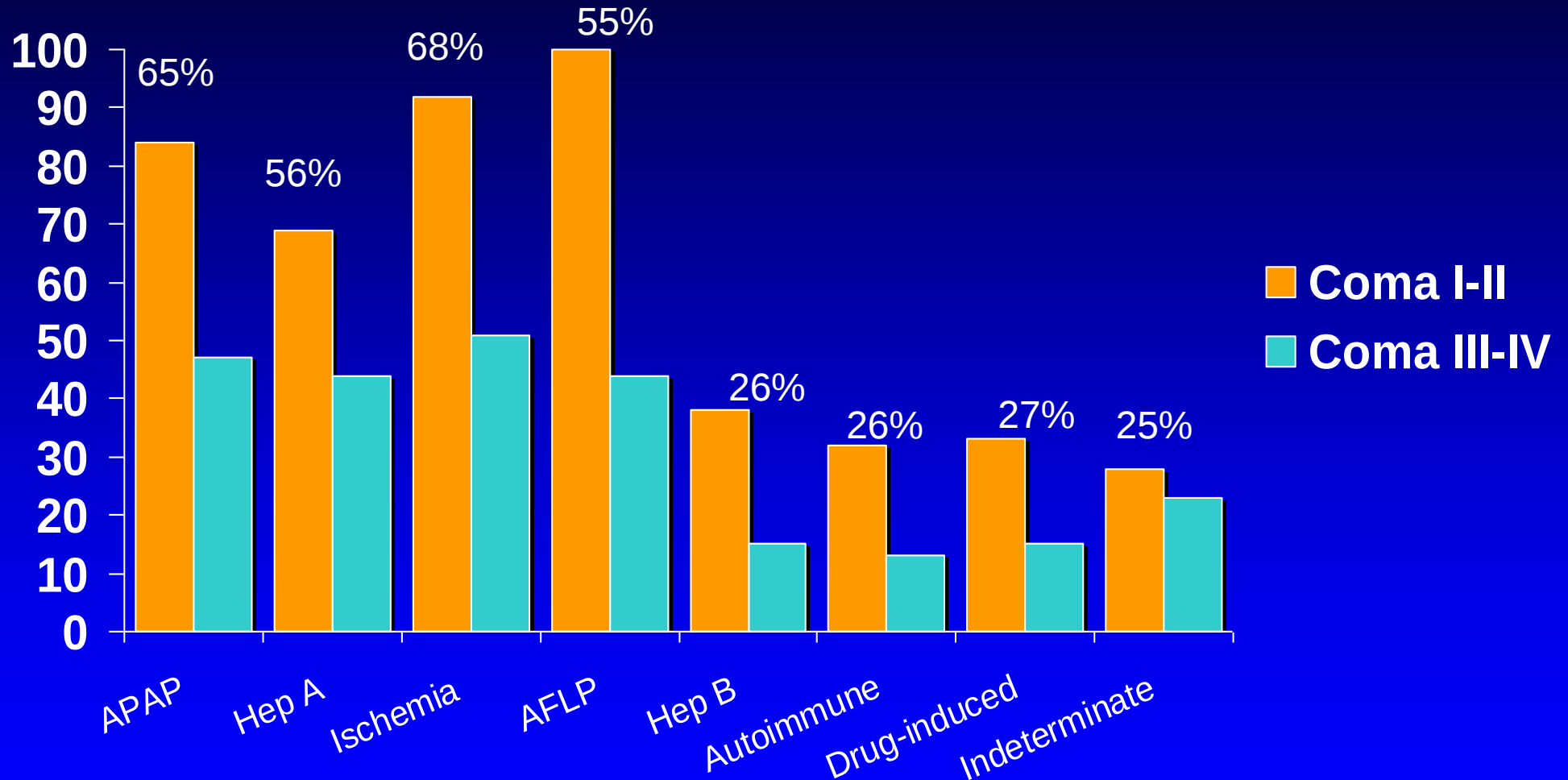
- Identification of any drug or toxin by history
 - Acetaminophen level and drug screen
- Viral hepatitis (Hep A IgM, HBsAg, anti-HBc IgM)
- Other rare causes
 - Autoimmune hepatitis (autoAb, γ -globulin, bx)
 - Pregnancy-related liver failure
 - HSV/ CMV, malignant infiltration (PCR, bx)
 - Wilson- ceruloplasmin, 24 hr urine Cu, slit-lamp
 - Budd-Chiari (USN doppler)
 - Rhabdomyolysis/ heat stroke/ ischemia

ALFSG '98-'07 n= 1,033 adults



(Fontana Sem Liv Dis 2008)

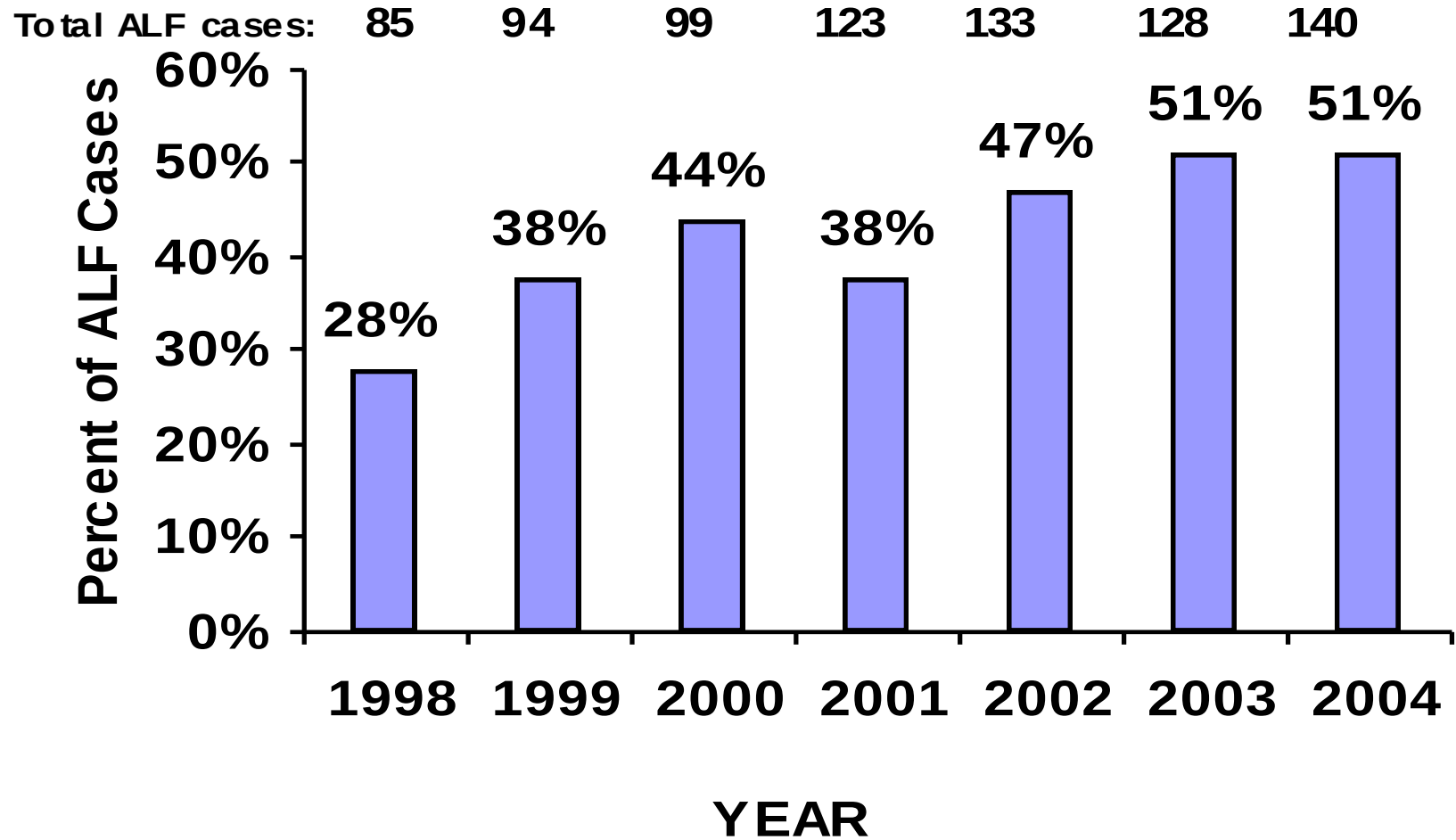
Transplant-free survival by etiology and coma grade



Treatable causes of FHF

<u>Diagnosis</u>	<u>Treatment</u>
Acetaminophen	Lavage, charcoal, N-acetylcysteine
Amanita	Lavage, IV Penicillin, dialysis
Autoimmune hepatitis	Steroids
Budd-chiari	Anticoagulation
Hepatitis B	Entecavir
Herpes simplex	Acyclovir
Pregnancy	Delivery
Wilson's disease	? Chelation, plasmapheresis

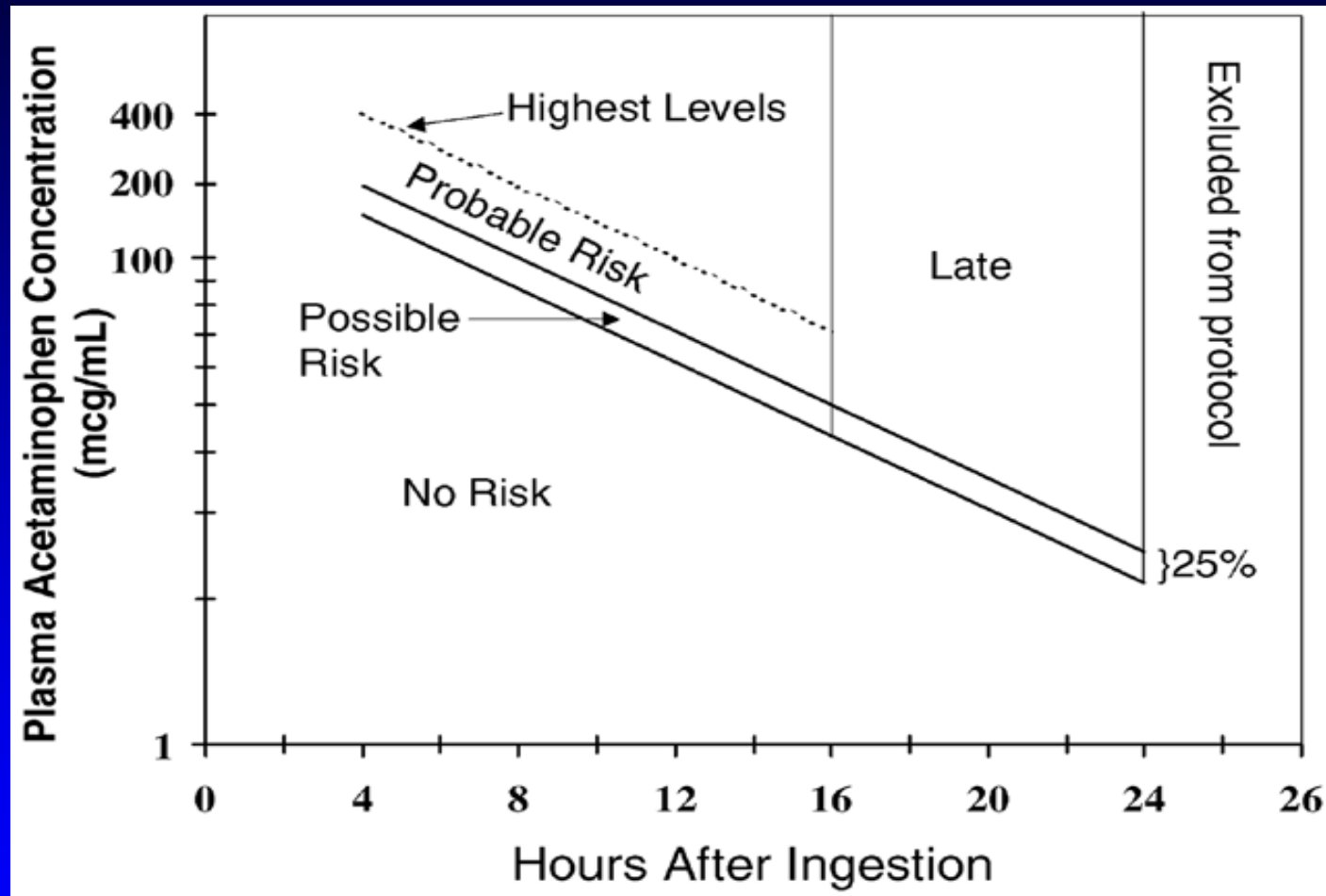
% Acetaminophen ALF in the US



Diagnosis of Acetaminophen Hepatotoxicity

- History of potentially toxic ingestion
 - ? > 6 grams single dose
 - ? Chronic dosing
 - ? Fasting ? Alcohol
- High AST & ALT (> 1,000 IU/ml)
 - Exclude other causes
- Serum ACM level (Nomogram)
 - False + with some colormetric assays

Serum Acetaminophen nomogram



All received oral NAC, < 1 % died
ALT > 1,000 ~ delay in NAC (0% if < 8 hr)

(Rumack Arch Int Med 1981; 141)

N-Acetylcysteine

- Enhances glutathione stores
- Oral NAC for ACM overdose
 - 140 mg/kg then 70 mg/kg q 4^o to 72 hrs or INR < 1.5
 - 10-20% nausea / vomiting
- IV NAC (Acetadote®)
 - Short gut, ileus, pregnancy
 - 150 mg/kg in D₅W (1 hr) 50 mg/kg (4 hr) 125 mg/kg (19 hr)
 - Hypersensitivity reaction 3%
- **Contraindication:** Sulfa-allergy, arrhythmia

Acetaminophen ALF in the US

	Intentional (n=122)	Non-intentional (n=131)
Serum ALT	5326	3319 *
Total ACM (g)	29	34
Serum ACM	95	42
% ≥ 2 ACM formul.	5%	38% *
% Narcotic-ACM	18%	63%* ^
% Listed / Txp	25%/ 7%	27%/ 9%
% Survival	71%	72%

* P < 0.05 ^ 70% Vicodin

(Larson Hepatology 2005; 42:1364)

General Measures for all FHF Patients

Monitor blood tests every 8 hours

Liver biochemistries, INR, Factor V

Electrolytes and renal function

ABG, arterial lactate, NH_3

Blood sugar monitoring (D_{10} or D_{50})

Liver biopsy not indicated for prognosis

Infection in FHF Patients

- **Daily surveillance cultures recommended**
 - Bacterial in 80%
 - Bacteremia in 25% (Staph, strep, GNR)
 - Respiratory, GI, and urinary pathogens
 - Fungal in 20% (fever, hypotension, ↑↑ WBC)
- **Preemptive broad-spectrum antibiotics**
 - Cephalosporin/ quinalone + vancomycin
 - Avoid aminoglycosides
 - Fever can worsen HE (SIRS)
 - Cooling blankets to < 100° F

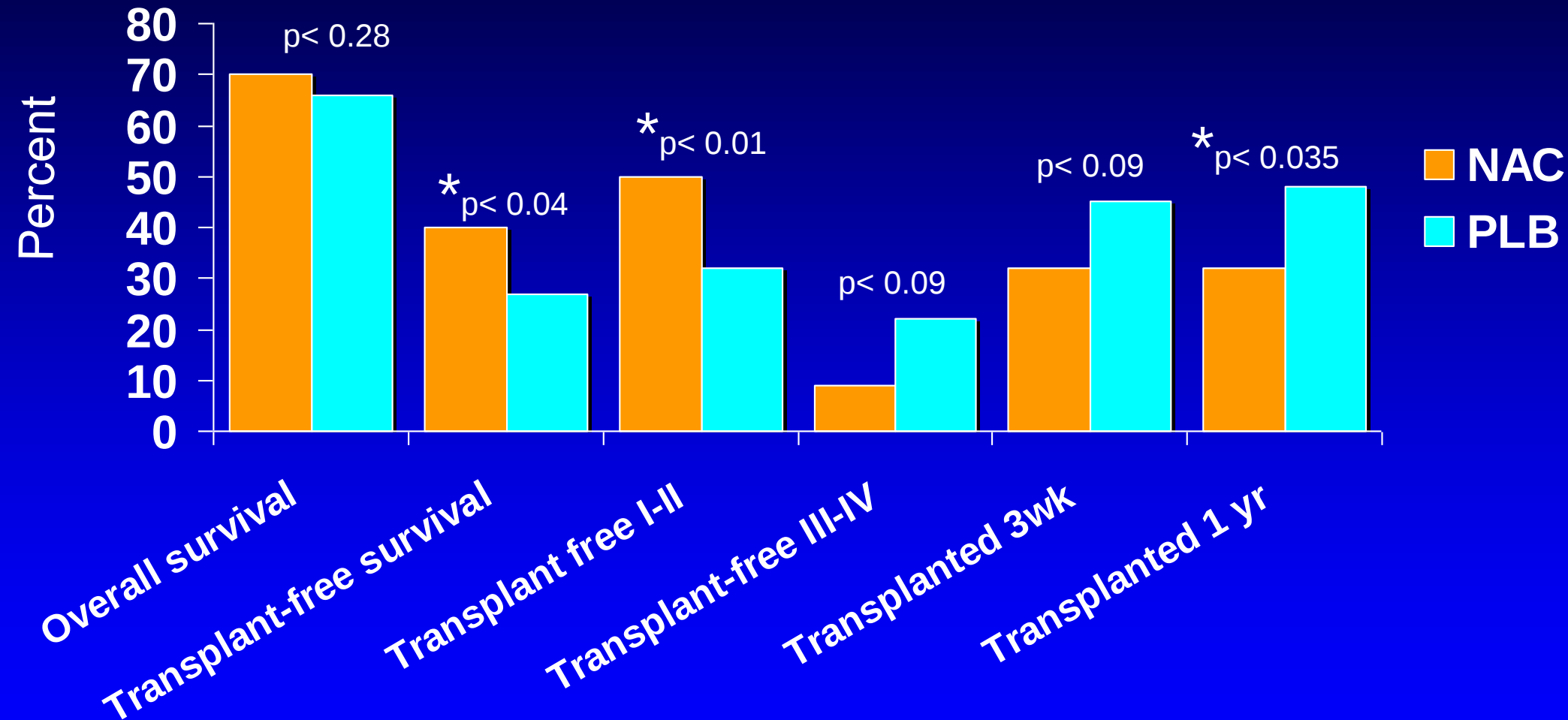
Coagulopathy in FHF Patients

- Multi-factorial etiology
 - Thrombocytopenia- liver, drugs, portal HTN
 - Hypoprothrombinemia (Vitamin K)
 - DIC
- Bleeding in ~ 10%
 - GI tract, mucosal surfaces
 - Recommend PPI or H₂ blocker
- Transfuse only if active bleeding/ procedure
 - FFP to INR < 1.5, platelets > 50 k
 - Cryoppt to fibrinogen > 100 mg/dl

A multi-center, randomized, double blind study of IV NAC vs. placebo for non-acetaminophen ALF

- **173 patients enrolled from 828 screened over 8 yrs**
Main groups: AIH, DILI, Hep B, Indeterminate
Randomized by site, coma grade (I-II vs III-IV)
Continued with standard care including OLT
- **Primary outcome: overall survival at 3 weeks**
- **Secondary outcomes: transplant-free survival, transplantation rate, length of ICU/hospital stay, number of organ systems failing**
- **Projected overall survival: 57% PLB vs 75% NAC (n=170)**

Primary/secondary outcomes in the NAC trial



Greatest difference in Txp-Free survival in grades I-II.

IV NAC for non-acetaminophen ALF

- No improvement in overall 3 wk survival with IV NAC vs PLB
 - Significant improvement in transplant-free survival (0.04).
 - Particularly for coma grade I-II ($p=0.01$, 2/3 of patients)
- Trend toward a difference in LOS, not in organ failure events
 - NAC was generally well tolerated
- **NAC can be recommended for early stage ALF in adults**
 - Pediatric RCT: No 1-yr survival benefit (73% vs 82%)
 - Lower 1-yr Txp-free survival (35% vs 53%, $p=0.03$)

Liver Transplant Evaluation

- **Hepatology / Transplant Surgery**
 - Diagnosis/ prognosis
 - Compliance
 - Medical co-morbidities
- **HIV, CMV, HSV, HepA IGM, HBsAg, HBcAb**
- **ID: Blood / fluid cultures, PPD**
- **Imaging: CXR, liver USN**
- **Cardiac: EKG, bedside 2D-Echo**

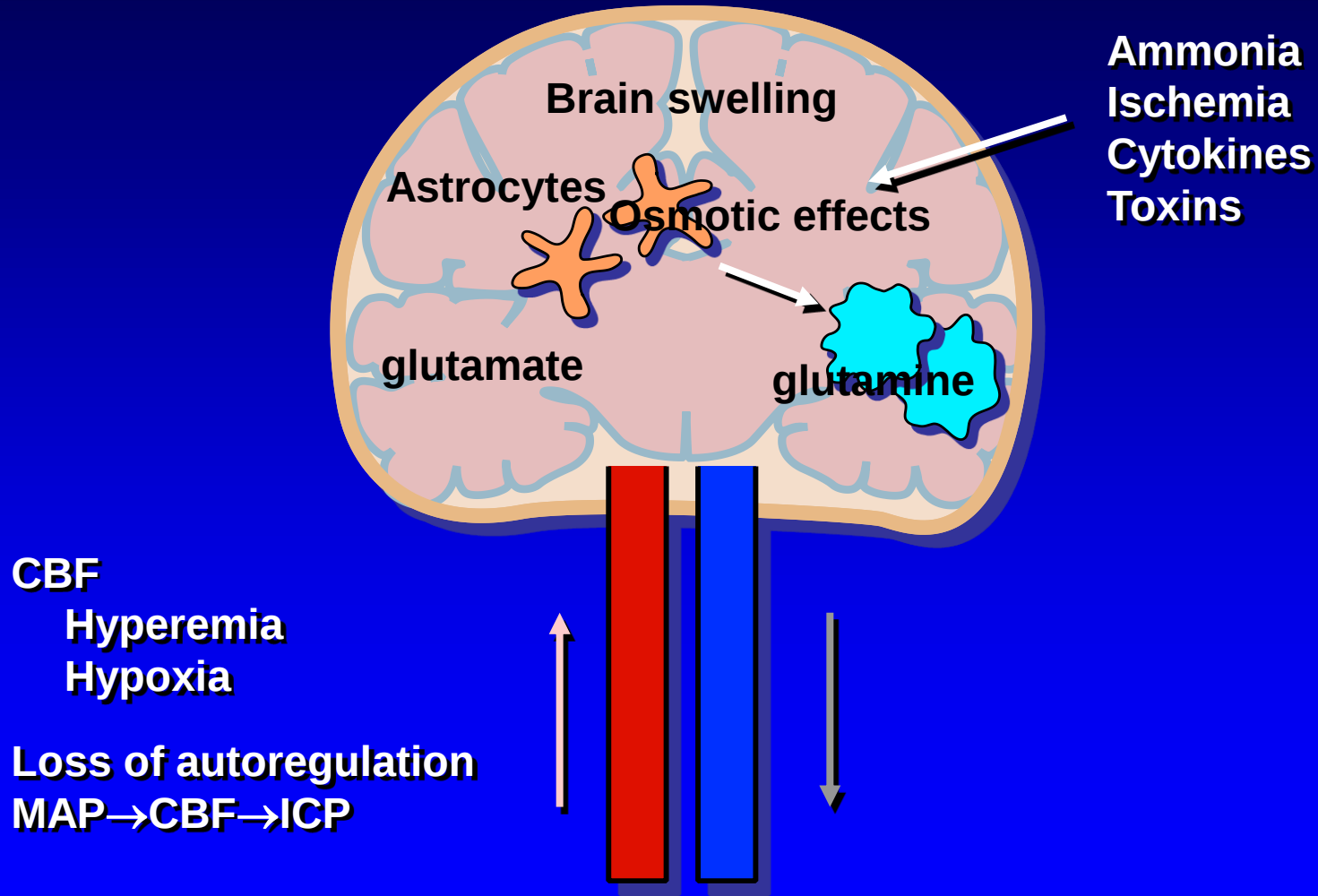
Intensive Care With Grade of Encephalopathy

Prevention and Treatment of Cerebral Edema

Cerebral edema

- Main cause of death in ALF
- Most likely in most “acute” cases
- Residual neurologic injury
- Requires management of hemodynamic, respiratory, cerebral and renal factors

Cerebral Edema in ALF



Intensive Care With Grade of Encephalopathy

Prevention and Treatment of Cerebral Edema

Grade I: Slow mentation with minimal change in level of consciousness

- Experienced nursing in quiet environment
 - Avoid sedatives/ hypnotics
- Identify etiology
 - OLT candidacy

Intensive Care With Grade of Encephalopathy

Prevention and Treatment of Cerebral Edema

Grade II: Gross disorientation, drowsiness, asterixis, inappropriate behavior

- Head CT
- Propofol or midazolam for severe agitation
- Antibiotics/ prognosis
 - Multiorgan failure

Intensive Care With Grade of Encephalopathy

Prevention and Treatment of Cerebral Edema

Grade III: Marked confusion, incoherent speech, sleeping most of the time but arousable to vocal stimuli

- Mechanical ventilation
- Hemodynamic and renal monitoring
- ICP monitoring and treatment
- Seizure management
- Prognostic assessment and timing of OLT

Hemodynamic Monitoring & Management

- PA catheter if hypotension, pressors, oliguria
 - Manage volume status to avoid worsening cerebral edema vs hypotension
 - Renal failure in 50% (poor prognosis)
 - CVVHD preferred over HD
- Maintain CPP > 60 (CPP = MAP-ICP)
 - Levophed preferred over vasopressin
- Quiet setting- avoid straining, valsalva, suctioning
 - Head of bed > 20-30°
 - Low PEEP ventilation

ICP Monitoring in ALF

Advantages:

- Discrepancies between clinical signs/ CT and ICP
- Sedation on ventilator makes neurologic assessment difficult
- No reliable signs of ↑ ICP during or after OLT

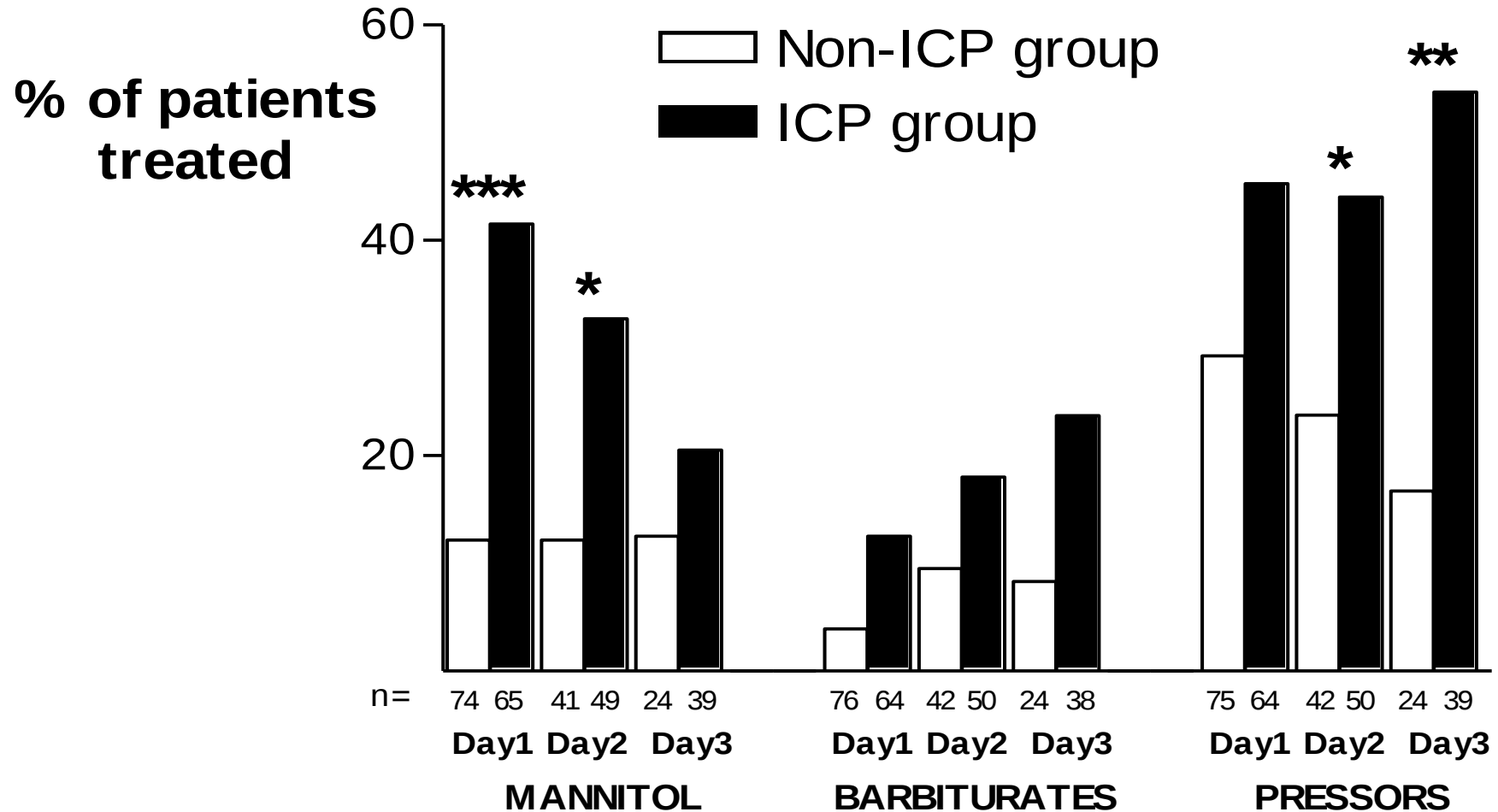
But:

- Treated patients survive longer but overall surv unchanged
- Potential bleeding complications

ICP monitoring in Grade $\frac{3}{4}$ HE

	No ICP N=240	+ ICP N=92	p
Age	40 + 14	36 + 12	< 0.01
INR	3.6 + 3.0	3.3 + 3.0	NS
Intubated	85%	100%	< 0.001
CVVHD	31%	60%	< 0.001
Listed for LT	31%	74%	< 0.001

Interventions for cerebral edema



ICP Monitor Protocol

- **Consult Neurosurgery if Grade 3/4 HE**
 - Non-contrast head CT
 - Platelets > 50 k
 - Cryoppt if fibrinogen < 100 mg/dl
 - 4 units FFP if INR > 1.5 *
 - Perioperative antibiotics

* rFVIIa only if refractory

rFVIIa Protocol

- Localized clot formation with tissue factor
 - 100% vs 0% INR correction
 - 100% vs 38% ICP placed
- **Contraindications:** Budd chiari, cancer, DVT/thrombophilia, pregnancy
- Must receive FFP first
- **rFVIIa 80 ug/kg *** bolus over 5 min
 - 4 -6 hour window

* \$5,000/ dose; not FDA approved

(Shami Liver Transplantation 2003)

Treatment of Cerebral Edema

CPP < 50 or ICP > 25 for 5 min

- Hyperventilate to PaCO₂ of 25 mmHg
- IV mannitol 0.5-1 g/kg bolus over 5 min
 - **Monitor serum osmolarity/ osmolar gap**
 - **? Renal failure dosing/ hypertonic saline**
- Pentobarbital coma 100-150 mg bolus over min
 - 1-3 mg/kg/ hr infusion
 - Hypotension

Treatment of refractory cerebral edema

- Hypothermia to 33° C
 - Cooling blanket vs intravascular vs arctic suit
 - 13 of 14 supported through OLT
 - Atricurium vs propofol to prevent shivering
- **Issues:** Coagulopathy, infection, cardiac
 - ? Rewarming
 - ? Liver regeneration
 - Need RCT with ICP monitoring

Modified King's College Criteria

(Bernal Lancet 2002; 359: 558)

- Acetaminophen
- Lactate > 3.5 in 4 hrs
- pH < 7.3 or lac > 3.0 in 12 hrs
- INR > 6.5
- Creatinine > 3.4
- Stage 3/4 HE
- Non-Acetaminophen
- INR > 6.5
- or 3 of the following
 - INR > 3.5
 - Age $< 10 > 40$
 - Bili > 17.5
 - Jaundice > 7 d
 - Etiology: drug rxn

Intensive Care With Grade of Encephalopathy

Prevention and Treatment of Cerebral Edema

Grade IV: Comatose, unresponsive to pain, decorticate or decerebrate posturing

- Management as in stage III
- ICP >MAP for 30 minutes, suspect irreversible brain damage
- Brain death by no cerebral perfusion on Tc99 brain scan
- Contraindications for OLT :
 - uncontrolled sepsis (not positive blood culture)
 - severe multiorgan failure/ refractory hypotension
 - uncontrolled intracranial hypertension
 - catastrophic lesion on head scan or brain death

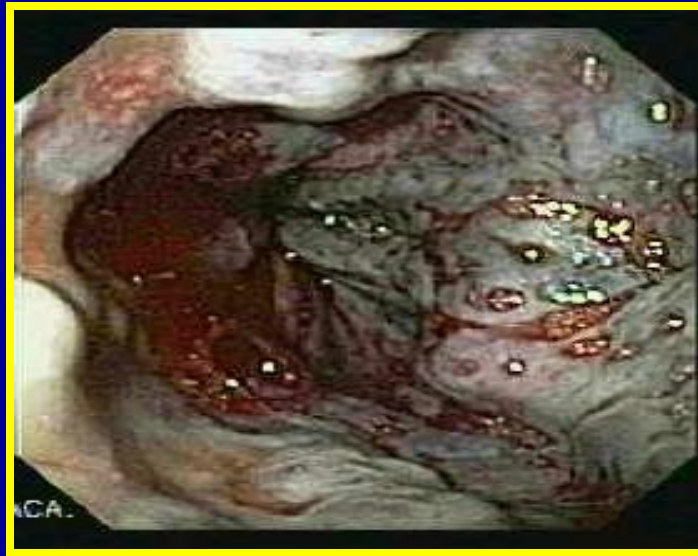
Liver Transplantation in ALF

- Early referral and evaluation
 - Status 1A listing
 - A, B, O compatible whole liver
 - 3.5 days to transplant
 - 200 transplant recipients/yr
- **75%** 1-year survival postOLT

Acute Liver Failure 2013

- **ALF is a rare but dramatic illness**
 - **Rapid diagnosis: treatment, prognosis**
 - **Give NAC to all suspected ACM overdose**
 - **NAC of probable benefit in early non-ACM**
- **Cerebral edema & sepsis**
 - **ICP monitors allow more intervention**
- **Liver transplantation is effective for selected patients but limited availability**

Management of Variceal bleeding



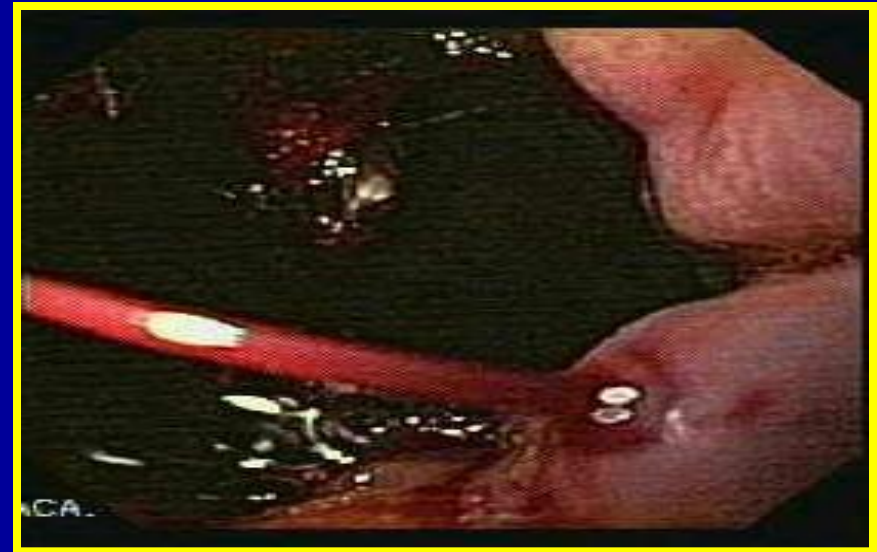
Robert J. Fontana, MD

Medical Director of Liver Transplantation

University of Michigan Medical School

Variceal bleeding

- Pathophysiology
- ICU management
 - Blood products/antibiotics
 - Vasoconstrictors
 - Endoscopy
- Refractory bleeding
 - Balloon tamponade
 - TIPS



Case #1

- A 40 year old alcoholic brought to ER with hematemesis and confusion.
- PE: Orthostatic, asterixis, black stool on rectal
 - Hgb 9 Plt 50 k Bili 10 INR 2.0
 - Resuscitated with IV fluids; IV Unasyn.
- **EGD-** 3 large esophageal varices with red wales, diffuse portal gastropathy but no active bleeding.

Case #1

- The most appropriate management of his variceal bleeding is:
 - Variceal Banding alone
 - Variceal Banding + octreotide
 - TIPS
 - Surgical shunt

Variceal bleeding overview

- **30% -70% of cirrhotics have varices (6%/yr)**
 - **30% bleed**
 - Risk ~ Variceal size, red wales, CTP C
 - Tension = rad x pres/ wall thickness
 - **< 50% stop bleeding spontaneously**
 - PRBC = 4 (0-60)
- **20% in-hospital mortality**
 - **Liver disease severity**
 - Aspiration, encephalopathy, sepsis, ARF
 - **30-50% 1 yr mortality**

Evidence based management

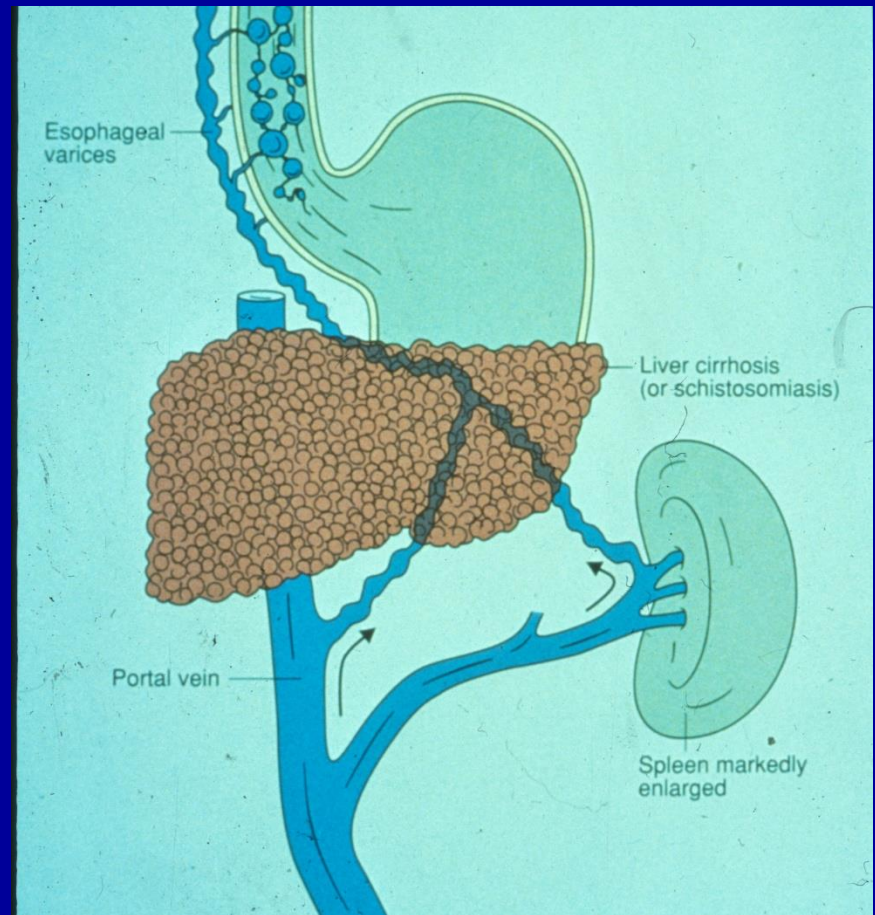
Variceal bleeding

+ Benefit	No benefit
Antibiotics (↓ Infxn, ↑ survival)	Sucralfate
Endoscopy (↓ Bleed, rebleed)	rFVIIa
Vasoactive drugs (↓ Txf, bleed)	
1 ° & 2° B-blocker (↓ Bleed, rebleed)	

? Proton pump inhibitors

Portal Hypertension

- Prehepatic, **hepatic**, post-hepatic
 - ↑ resistance to blood flow
- Cirrhosis
 - Distorted microarchitecture
 - Esophagogastric varices
- Portosystemic gradient
 - Wedge – free HV pressure
 - > 12 mm Hg



UGI Bleeding in cirrhosis

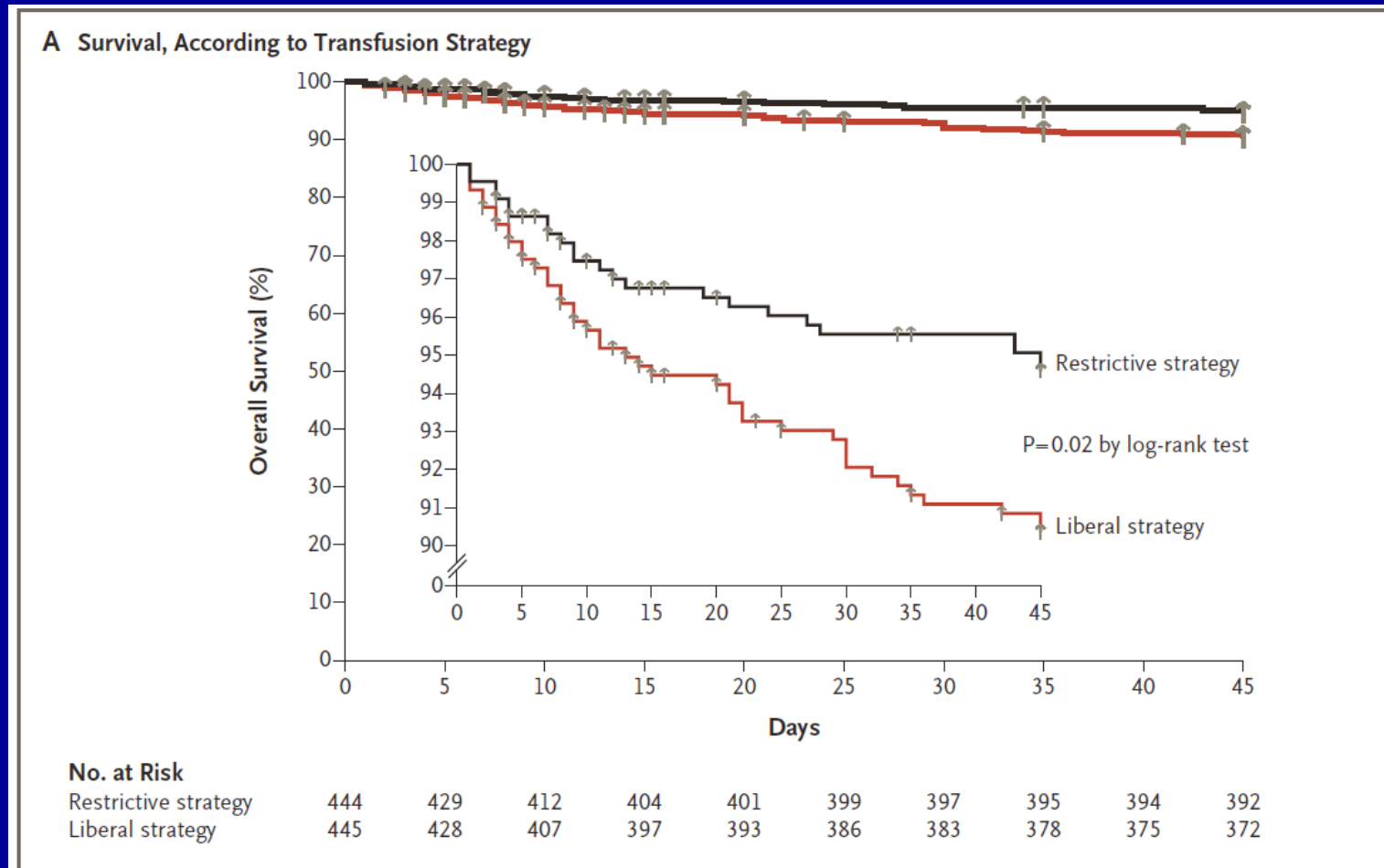
- **Resuscitation: 2 large IV/ central access**
 - FFP to keep INR < 1.5, platelets > 50 k
 - Target hemoglobin ~ **7 to 9 g/dl**
 - Hypertransfusion can ↑ portal pressure
- **NG tube for gastric lavage**
 - IV or oral PPI
 - 25% non-variceal
 - IV erythromycin (125 mg) or IV reglan (10 mg)
- **ICU monitoring**
 - Intubate if aspiration/ encephalopathy

Transfusions in UGI bleeding

Barcelona 2003 to 2009

	Restrictive (n=444) Hgb 7 to 9	Liberal (n=445) Hgb 9 to 11
Bleeding source		
PUD	51%	47%
GE varices	23%	24%
Others	27%	29%
Cirrhosis	139 (31%)	138 (31%)
A	37 (27%)	30 (22%)
B	76 (55%)	79 (57%)
C	26 (19%)	29 (21%)
HVPG (mm Hg)	20.1 + 4.4	20.6 + 5.2
PRBC (%)	219 (49%)	384 (86%)
Mean/pt	1.5 + 2.3	3.7 + 3.8
Total colloids in 72 hrs (ml)	5491	5873

Transfusions in UGI Bleeding



Survival improved cirrhotics HR: 0.30 (0.011 -0.85)

(Villanueva NEJM 2013; 368: 11-21)

Infections with variceal bleeding

- 20% infected at admission
 - 70% in-hospital
 - Urine, ascites, respiratory
- Broad spectrum antibiotic X 5 to 10 days
 - ↓ Infections RR= 0.40 (CI 0.32-0.51)
 - ↓ **Mortality RR= 0.75 (CI: 0.55 -0.95)**
- Greatest benefit in Child's C and pre-EGD
 - Cefotaxime, levaquin, unasyn

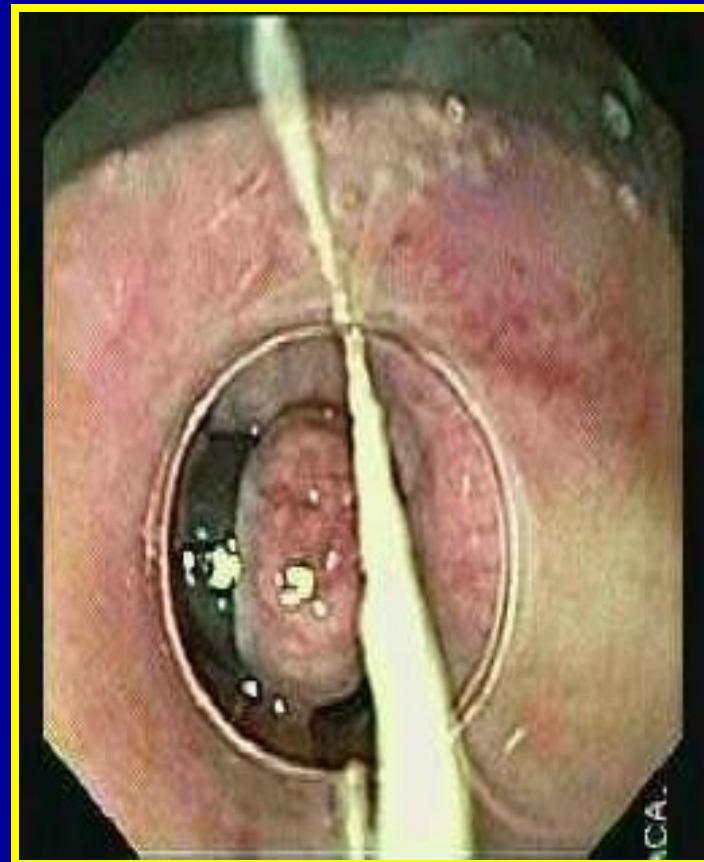
Pharmacological therapy

Splanchnic vasoconstrictors

- Sandostatin (**Octreotide**) (↓glucagon)
 - 50 ug bolus and 50 ug/hr x 5 days
 - Octreotide vs vasopressin
 - Bleeding control RR= 1.62 (1.37-1.93)
 - Side effects (0% vs 10%)
 - Octreotide vs sclerotherapy
 - Similar bleed control, rebleeding, mortality
 - Octreotide + sclero/ banding vs EGD
 - ↑ bleed control, ↓ rebleed: no effect on mortality
- Vasopressin + IV NTG

Emergent EGD in variceal bleeding

- **IV sedation vs intubation**
 - Varix size/ stigmata
 - Hemostasis in 80 -90%
- **Band ligation vs sclerotherapy**
 - Similar efficacy
 - ↓ infection
 - ↓ ulcers, strictures
 - Poorer visualization

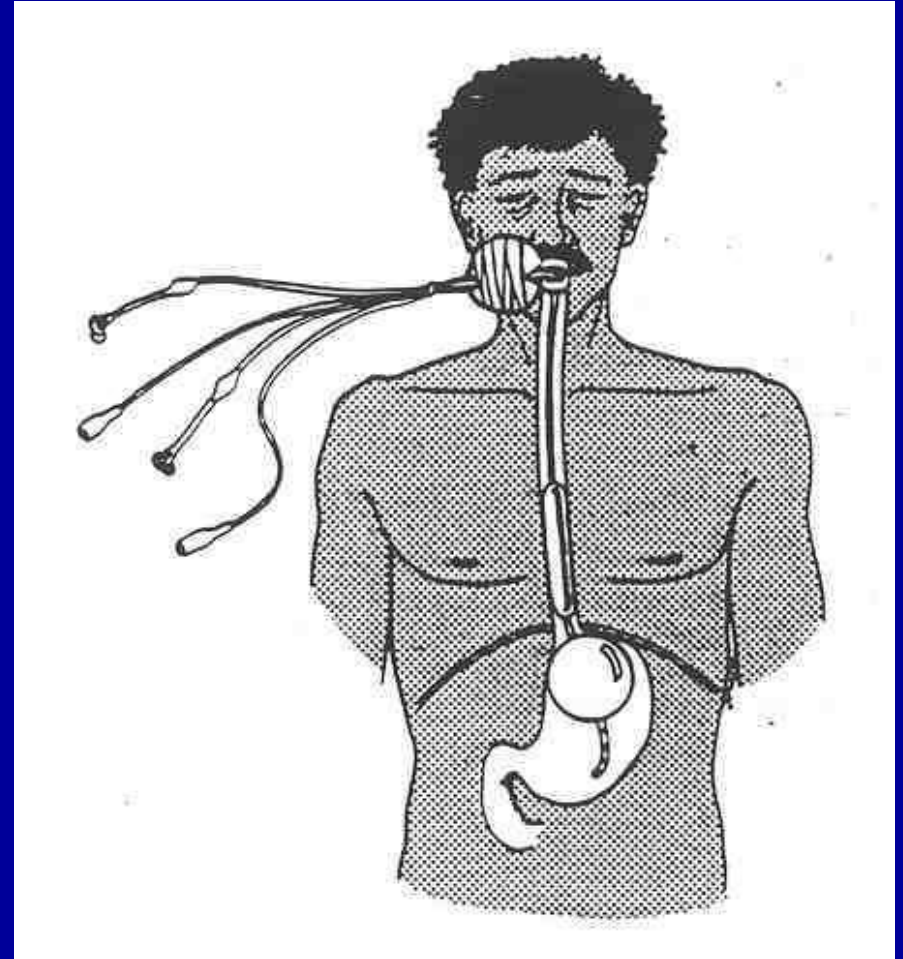


Early variceal rebleeding

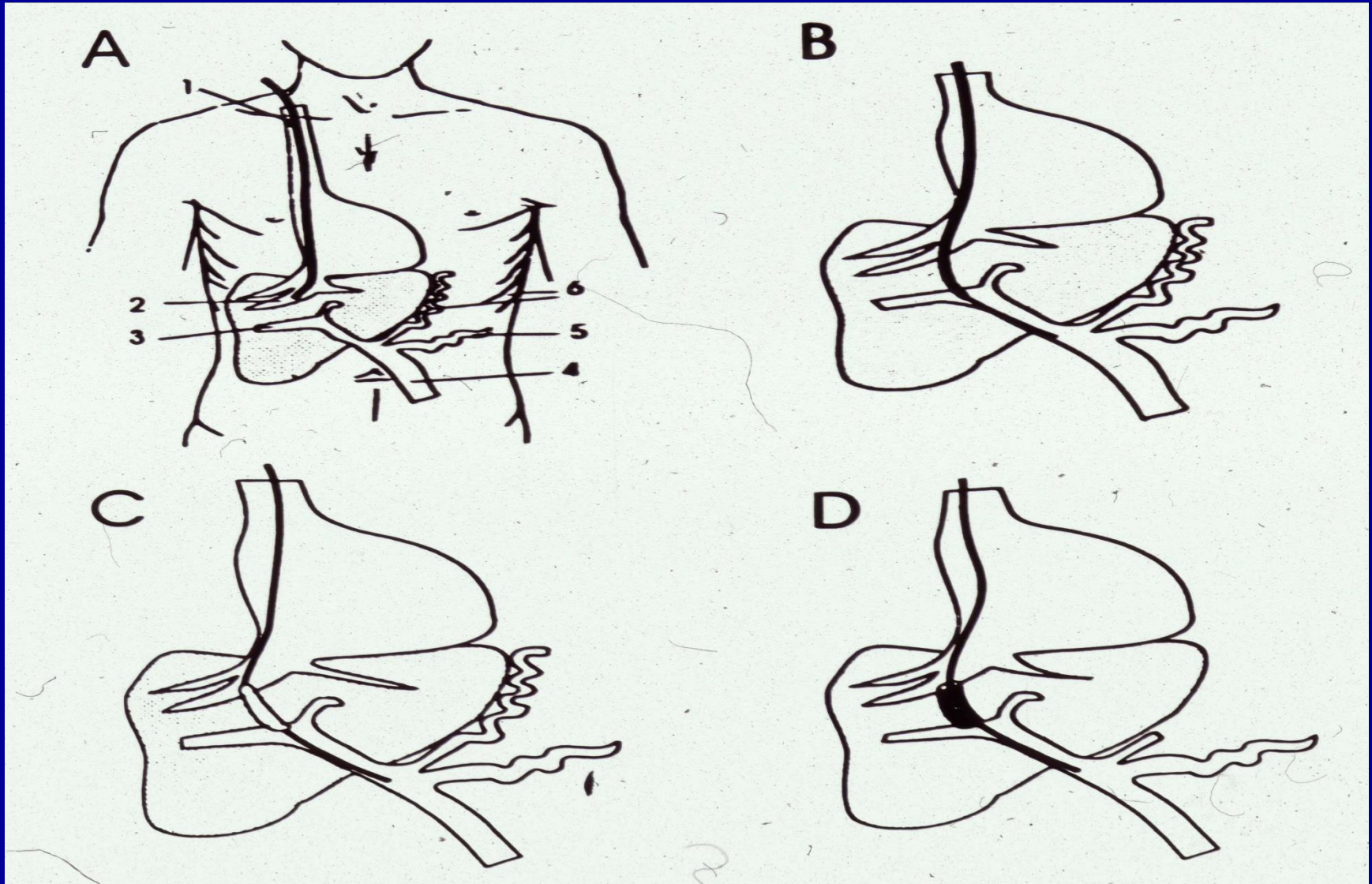
- Within 5 days (**10-20%**)
 - > 4 PRBC's or hypotension in 1st 6 hours
 - ↑↑ Risk: PV thrombus, HVPG > 20, infection
 - Continue octreotide
 - Antibiotics/ blood products
- Repeat EGD to identify source
 - Esophageal ulcers
 - Esophageal varices → Band/ sclero
 - Gastric varices → TIPS
 - Balloon tamponade to temporize

Blakemore/ Minnesota tube

- **Indication:** Failed EGD/vasconstrictors
- Intubate and sedate
 - Oral or nasal insertion
 - External fixation
 - x-ray confirmation
- Balloon tamponade
 - Gastric: 250 ml < 24 hr
 - Esophag: 100 ml < 12 hr
 - **90%** effective
- Complications **15%**
 - Esoph perf, ischemia



Transjugular Intrahepatic Portosystemic Shunt



Salvage TIPS for refractory variceal bleeding

- **Indication**
 - Persistent EV bleeding after EGD
 - Gastric varices with stigmata
 - Resuscitation/ stabilization prior to travel
- **Efficacy: > 95%**
- **Contraindication: ↑↑ risk/ ↓↓benefit**
 - CTP > 12 , MELD > 30
 - Multi-organ failure
 - RHF/ moderate pulm HTN *
 - Hepatoma/ PV thromboses *

* 2D- Cardiac echo, Liver USN + doppler

Prevention of variceal rebleeding

	Endo	Surgery	TIPS
Rebleeding	50% 47%	12% *	19%*
Encephalopathy	9% 19%	17% *	34%
Mortality	29% 27%	29%	27%

N= 376 Endo vs surgery (Meta-analysis Hepatology 1995; 22: 332)

N=811 Endo vs TIPS (Meta-analysis Hepatology 1999; 30: 612)

DSRS vs TIPS

140 Child's A/B

Mean f/u = 46 ± 26 months

	DSRS (n=73)	TIPS (n=67)
Rebleeding	5.5%	10.5%
Encephalopathy	50%	50%
Ascites (early)	29% (15%)	25% (0%)
2-yr survival	81%	88%
Reintervention	11%	82% *

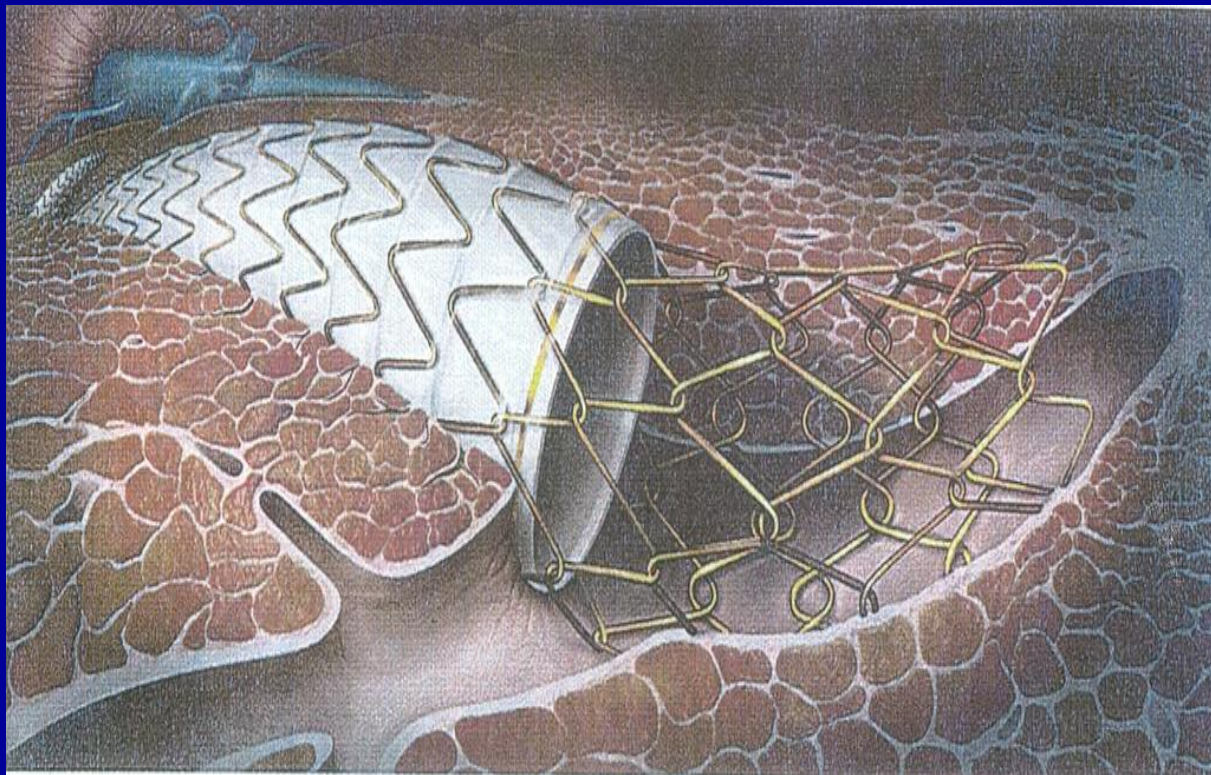
HRQOL, initial & total costs similar in both groups

(Gastroenterology 2006; 130)

Viatorr vs Wall Stent

80 cirrhotics with variceal bleeding or ref ascites

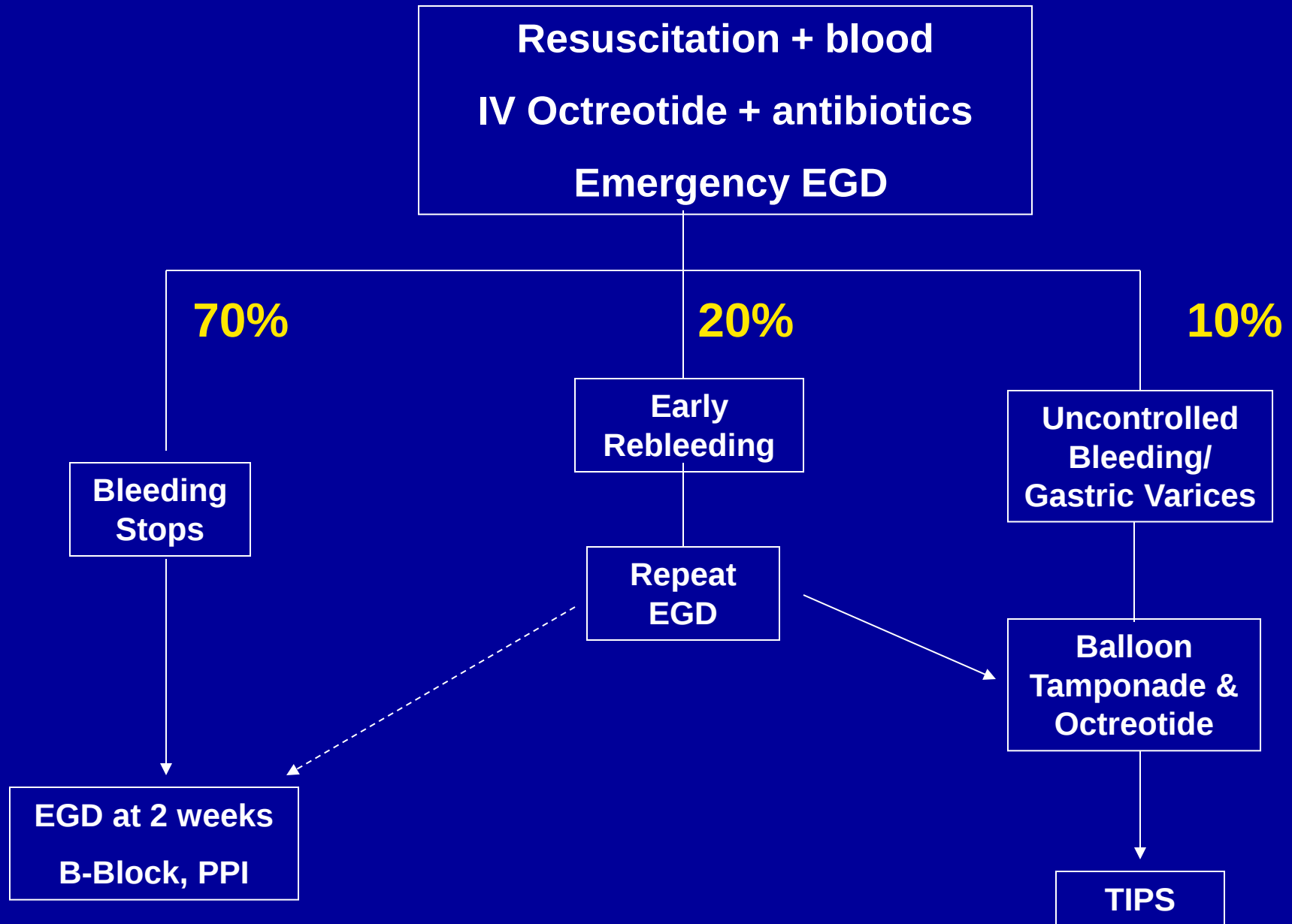
- **Shunt dysfunction 13% vs 44% ($p < 0.001$)**
- **1 year patency (venography) 86% vs 47%**
- **Similar rates of encephalopathy and survival**



Prevention of rebleeding

- **Follow-up EGD + banding**
 - Q 2 weeks till obliterated
 - PPI bid to ↓↓ esophageal ulcer bleeding
- **Non-selective B-Blocker**
 - ↓↓ Rebleed: 40% to 20%
- **Avoid ulcerogenic drugs**
 - ASA, NSAID's, fosamax, plavix
- **Liver transplant evaluation**

Management of Variceal Hemorrhage



Variceal bleeding in 2013

- Variceal bleeding can be life-threatening
 - Outcome: Cirrhosis severity, hemostasis
- Emergent EGD after resuscitation >90% efficacy
 - Antibiotics improve SURVIVAL
 - Octreotide preferred over vasopressin
 - Early rebleeding → repeat EGD
- For uncontrolled bleeding and selective rebleeders, balloon tamponade as bridge to TIPS.
- 2° prevention: Follow-up EGD, B-blockers, PPI and avoid ulcerogenic drugs

Prevention of Nosocomial Infections in the ICU

Daniel J. Morgan MD, MS
University of Maryland School of Medicine
VA Maryland Healthcare System
August 10, 2013

TOPICS

- Epidemiology of Healthcare-associated Infections (HAIs)
- MDROs and *C. difficile*
- Isolation Precautions
- Preventing & Treating HAIs
 - VAP
 - UTI
 - CLABSIs (later)
- Infection control potpourri

QUESTION 1

The national U.S. rates of which of the following healthcare-associated infections have increased during the past decade?

1. Surgical site infections
2. Central vascular catheter-associated bloodstream infections
3. *Clostridium difficile* infections
4. Catheter-associated urinary tract infections
5. Ventilator-associated pneumonias

Infection Control Over the Past Decade

	Rate	
Parameter	Then	Now
CLABSIs	5.0/1000 catheter days	1.7/1000 catheter days
VAP	9.5/1000 ventilator days	2.0/1000 ventilator days
CAUTIs	5.4/1000 catheter days	3.1/1000 catheter days
<i>C. difficile</i> infection	5.5 cases/ 10,000 discharges	11.2 cases/ 10,000 discharges

Abbreviations: CLABSIs: Central line associated bloodstream infections; VAP: ventilator-associated pneumonia; CAUTIs: catheter-associated urinary tract infections

In-patient Infections – “National” Surveillance

National Healthcare Safety Network (NHSN), Jan 2006 – Oct 2007

	Overall	CLABSI	CAUTI	VAP
Rank				
1	CoNS	CoNS	E coli	<i>S aureus</i>
2	<i>S aureus</i>	<i>Enterococcus</i> spp	<i>Candida</i> spp	<i>P aeruginosa</i>
3	<i>Enterococcus</i> spp	<i>Candida</i> spp	<i>Enterococcus</i> spp	<i>Enterobacter</i> spp, and <i>A baumannii</i>
4	<i>Candida</i> spp	<i>S aureus</i>	<i>P aeruginosa</i>	--

CLABSI: central-line associated bloodstream infection; CAUTI: catheter-associated urinary tract infection; VAP: ventilator-associated pneumonia; SSI: surgical site infection; CoNS: coagulase-negative Staphylococci.

➤ **48 hours inpatient = nosocomial/HAI!**

➤ **Healthcare-associated Infection (inpatient/outpatient)**

Hidron et al., *Infect Control Hosp Epidemiol* 2008; 29:996-1011.

Epidemiology of organisms – dumbed down

- *S. aureus* #1 real pathogen (50% MRSA) but declining
- Enterococcus/VRE slowly declining
- Gram-negatives (MDR gram negatives) increasing
- *C. difficile* increasing
- Candida increasing

Control & Prevention based on Modes of Transmission of Infectious Agents

- **Contact**
 - Direct (body-to-body)
 - Indirect (e.g., fomites/environment, HCWs' hands)
- **Large Droplet** ($>5\ \mu\text{m}$; travel 3-6 feet)
- **Small Droplet** (droplet nuclei $\leq 5\ \mu\text{m}$; remain **airborne**)

Contact Precautions

- VRE, MRSA, multiple antibiotic resistant gram negative rods, *Clostridium difficile**
 - most common form of isolation
- private room
 - cohort same organisms
- gloves & gowns for any contact with patient or environment

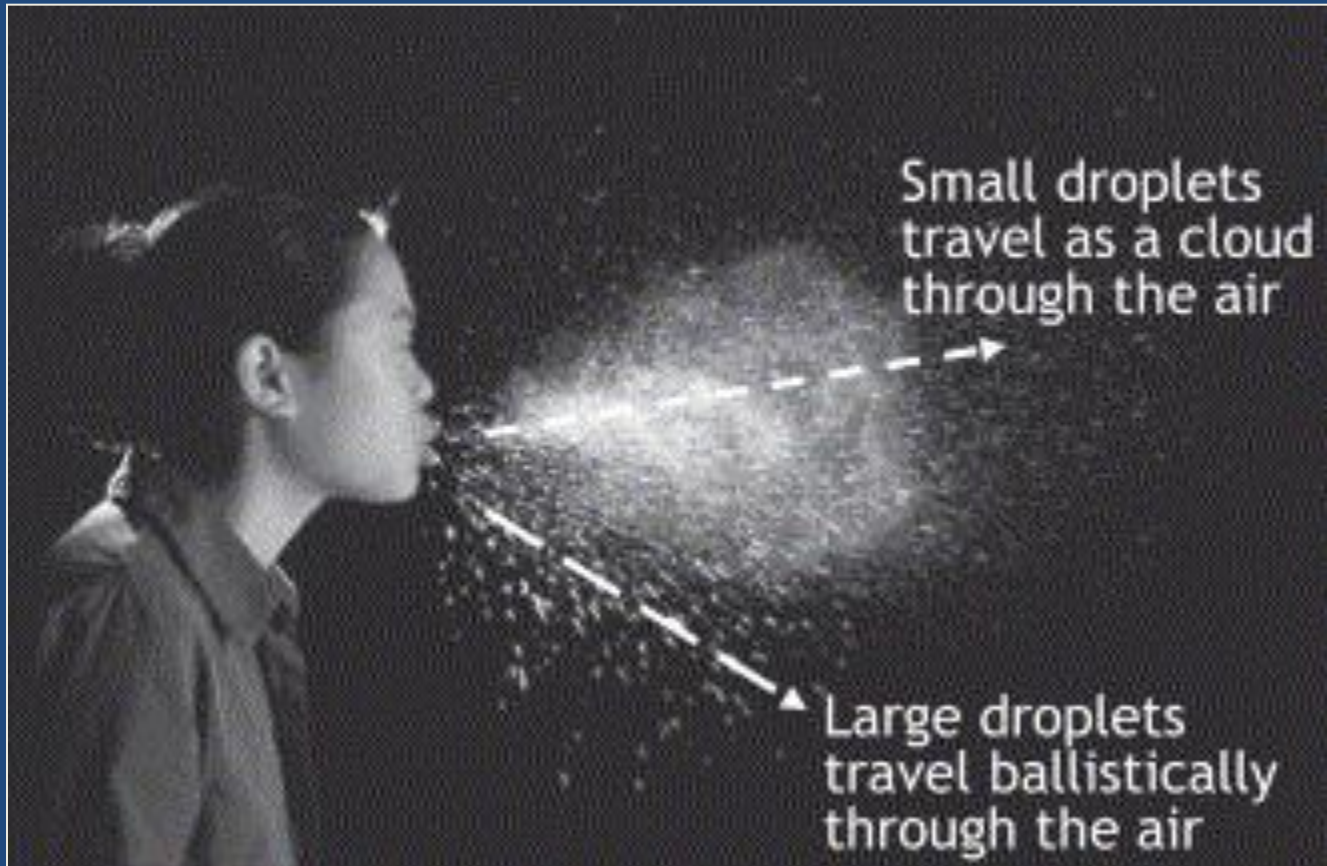


*wash hands with soap and water for *C. difficile*

QUESTION 2

The most appropriate hospital room placement for a patient with seasonal influenza is:

-
1. Any room. no special precautions once anti-viral therapy initiated
 2. Private room; personnel mask for patient contact (3-6 feet of patient)
 3. Private room; personnel must mask and gown to enter room
 4. Private room with negative pressure
 5. Private room with negative pressure and 100% exhaust (i.e., no recirculation of air)

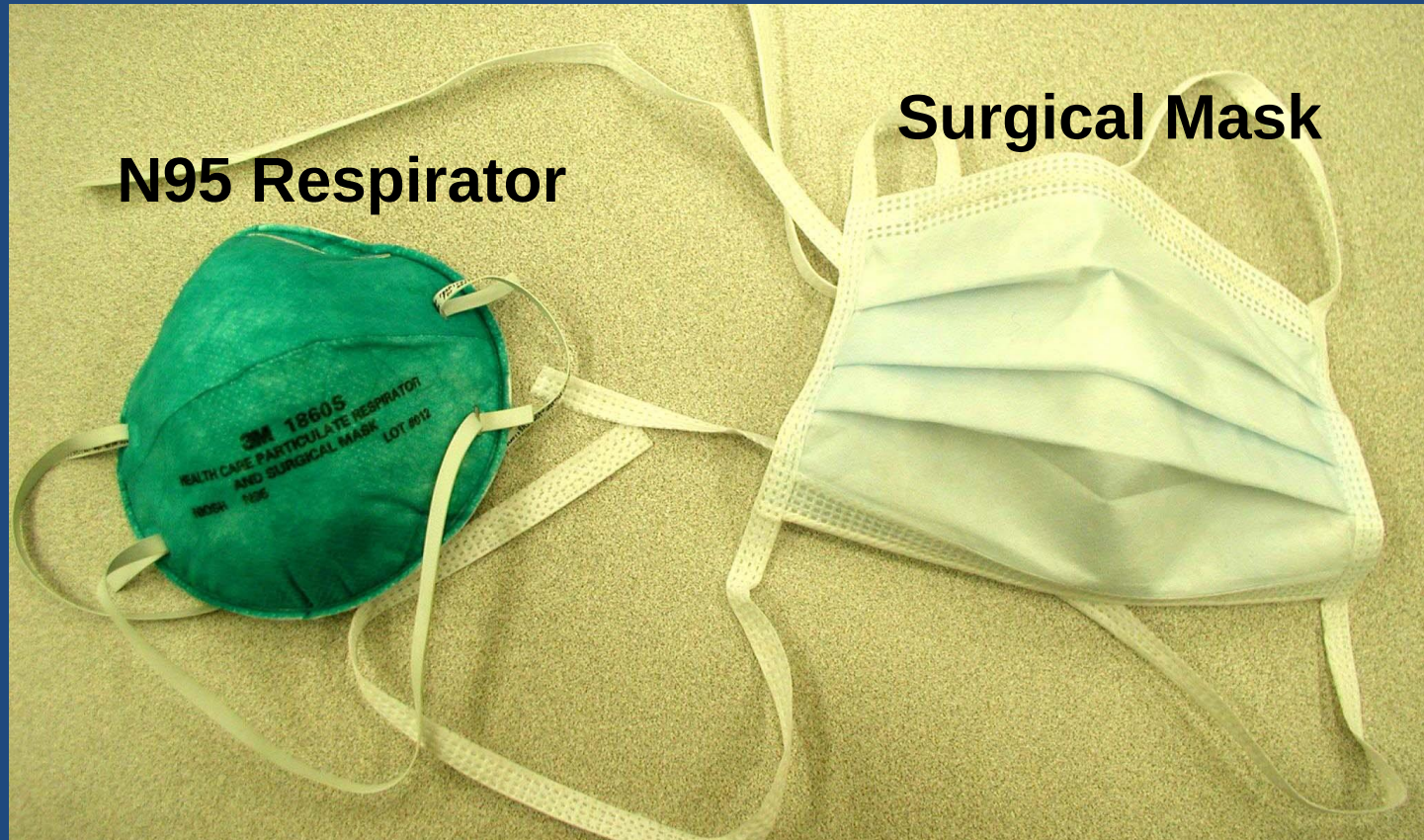


TB

Flu

Permission of Prof. Andrew Davidhazy, School of Photographic Arts and Sciences, Rochester Institute of Technology, Rochester NY, USA.

Respiratory Protection



N95 Respirator

Surgical Mask

Isolation Categories are Based on Modes of Transmission

	Hand Hygiene	Private Room	Gloves	Gown	Mask	Eye Protection
Standard	Yes	PRN	PRN	PRN	PRN	PRN
Droplet	Yes	Yes*	PRN	PRN	W/in 3 ft	PRN
Contact	Yes	Yes*	Yes	Yes	PRN	PRN
Airborne	Yes	All	PRN	PRN	N95	PRN

* When possible; cohort if not possible. Avoid rooming with immunosuppressed or high risk patients. All = Airborne Infection Isolation: negative pressure with no air recirculation (unless HEPA-filtered); 6-12 ACH.

QUESTION 3

You admit a patient with sepsis and a history of decubitus ulcer infection by methicillin-resistant *S. aureus*, vancomycin-resistant Enterococci, and carbapenem-resistant *K. pneumoniae*.

The appropriate patient care order is:

1. Standard precautions
2. Droplet precautions
3. Contact precautions
4. Airborne precautions
5. Contact and airborne precautions

Isolation Precautions — Examples of Indications

- **Standard** – All patients
- **Contact** – Multidrug resistant bacteria, infectious diarrhea, chickenpox
- **Droplet** – Bacterial meningitis, pertussis, mumps, seasonal influenza
- **Airborne** – Tuberculosis, chickenpox, measles

QUESTION 4

Intensive Care Unit (ICU) staff who cared the prior day for a patient with fever and headache learn that the patient has meningococcal meningitis.

Which of the following ICU personnel should receive post-exposure prophylaxis:

1. Intern who did the lumbar puncture
2. Nurse who took the patient's initial vital signs
3. Transporter who brought patient from ED to the ICU
4. Intern, nurse & transporter
5. None of them

Meningococcus Answer

No prophylaxis necessary

To whom do you give prophylactic antibiotics?

- “Intimate” contacts only
 - Commonly: Household members, “Significant others”, Daycare contacts
 - Rarely: Healthcare workers
 - UNPROTECTED EXPOSURE TO RESPIRATORY SECRETIONS

PEP—1 prevention/144,000 contacts

(Gilmore, Lancet 2000)

Why do you give prophylactic antibiotics?

- The attack rate for household contacts is ~ 4 cases per 1,000 persons exposed
 - 500-800 times greater than for the total population
- Risk ratio for prophylaxis was 0.11
 - reduced the risk of secondary infection by 89%
 - number of contacts treated to prevent one secondary case was ~ 218

Multidrug-resistant Organisms (MDROs)

MRSA & VRE

- Gram-positive organisms
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-resistant Enterococcus (VRE)

Effective Antibiotics	
MRSA	VRE
Vancomycin	
Linezolid	Linezolid
Daptomycin	Daptomycin
Tigecycline	Tigecycline
Clindamycin/ doxycycline/ bactrim	
Ceftaroline	

MRSA & VRE

Pathogen	Overall ^a		CLABSI	
	No. (%) of pathogenic isolates	Rank	No. (%) of pathogenic isolates	Rank
CoNS	5,178 (15.3)	1	3,900 (34.1)	1
<i>Staphylococcus aureus</i>	4,913 (14.5)	2	1,127 (9.9)	4
<i>Enterococcus</i> species		3		2
<i>E. faecalis</i>	1,177 (3.5)		627 (5.5)	
<i>E. faecium</i>	1,888 (5.6)		942 (8.2)	
NOS	1,028 (3.0)		265 (2.3)	
<i>Candida</i> species		4		3
<i>C. albicans</i>	2,295 (6.8)		673 (5.9)	
Other <i>Candida</i> spp. or NOS	1,333 (3.9)		669 (5.9)	
<i>Escherichia coli</i>	3,264 (9.6)	5	310 (2.7)	8
<i>Pseudomonas aeruginosa</i>	2,664 (7.9)	6	357 (3.1)	7
<i>Klebsiella pneumoniae</i>	1,956 (5.8)	7	563 (4.9)	5
<i>Enterobacter</i> species	1,624 (4.8)	8	443 (3.9)	6
<i>Acinetobacter baumannii</i>	902 (2.7)	9	252 (2.2)	9
<i>Klebsiella oxytoca</i>	359 (1.1)	10	99 (0.9)	10
Other	5,267 (15.6)		1,201 (10.5)	
Total	33,848 (100)		11,428 (100)	

NOTE. Of the 28,502 cases of HAI reported, 4,671 (16.4%) were polymicrobial. associated bloodstream infection; CoNS, coagulase-negative staphylococci; NOS, no pneumonia.

^a The overall total includes data for 58 pathogens associated with postprocedural dependent on the relative amount of data submitted for each type of HAI.

Frequency of gram-negative rods

Pathogen	Overall ^a		CLABSI	
	No. (%) of pathogenic isolates	Rank	No. (%) of pathogenic isolates	Rank
CoNS	5,178 (15.3)	1	3,900 (34.1)	1
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MDR Acinetobacter/Carbapenem Resistant Enterobacteriaceae (CRE)

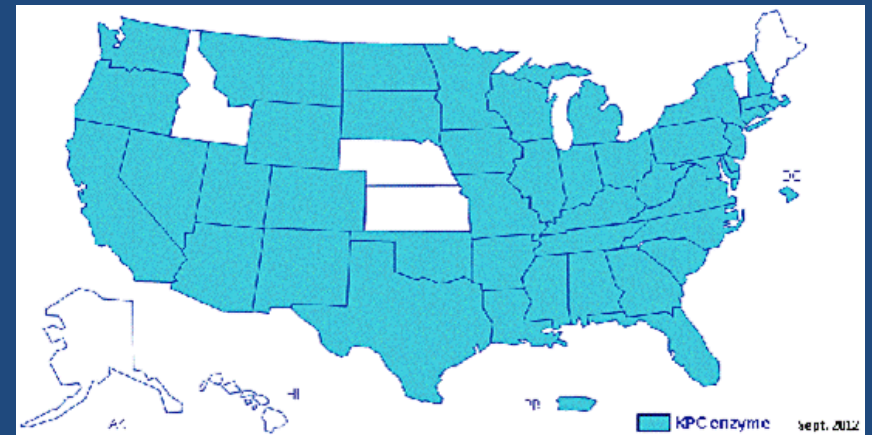
- Sensitive to ≤ 2 antibiotic classes not including tigecycline or polymyxin
- Resistant to Carbapenem antibiotics
- *Enterobacteriaceae*=
 - *Klebsiella*
 - *E. coli*
 - *Enterobacter, Citrobacter, Serratia.....*

States with confirmed CRE cases

2010



2012



US Epidemiology of CRE

- 2007 CDC data, 8% of all *Klebsiella* isolates carbapenem resistant (under 1% in 2000)
- Spread by transfer of colonized patients
- Long Term Acute Care Hospitals (LTACHs) important

QUESTION 5

You are caring for a patient found to have a CRE *Klebsiella* in the blood. What is the best treatment?

- 1) Ampicillin/sulbactam
- 2) Tigicycline
- 3) Amikacin
- 4) Polymyxin
- 5) Ciprofloxacin & aztreonam

CRE Treatment

- Polymyxin (colistin) first choice
- Adjunctive/2nd line
 - Amikacin
 - Tigecycline
 - Continuous infusion imipenem

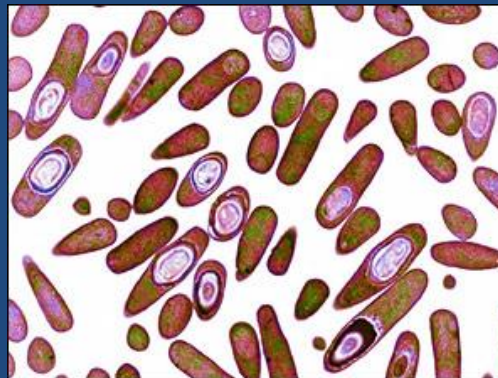
Clostridium difficile Infection (CDI)

- Antibiotic-associated diarrhea
 - Mild watery diarrhea to fatal
- Discovered in 1978 and evolving
- Clindamycin resistant outbreaks in 1990s
- Recent emergence of a more virulent strain



C. difficile pathogenesis

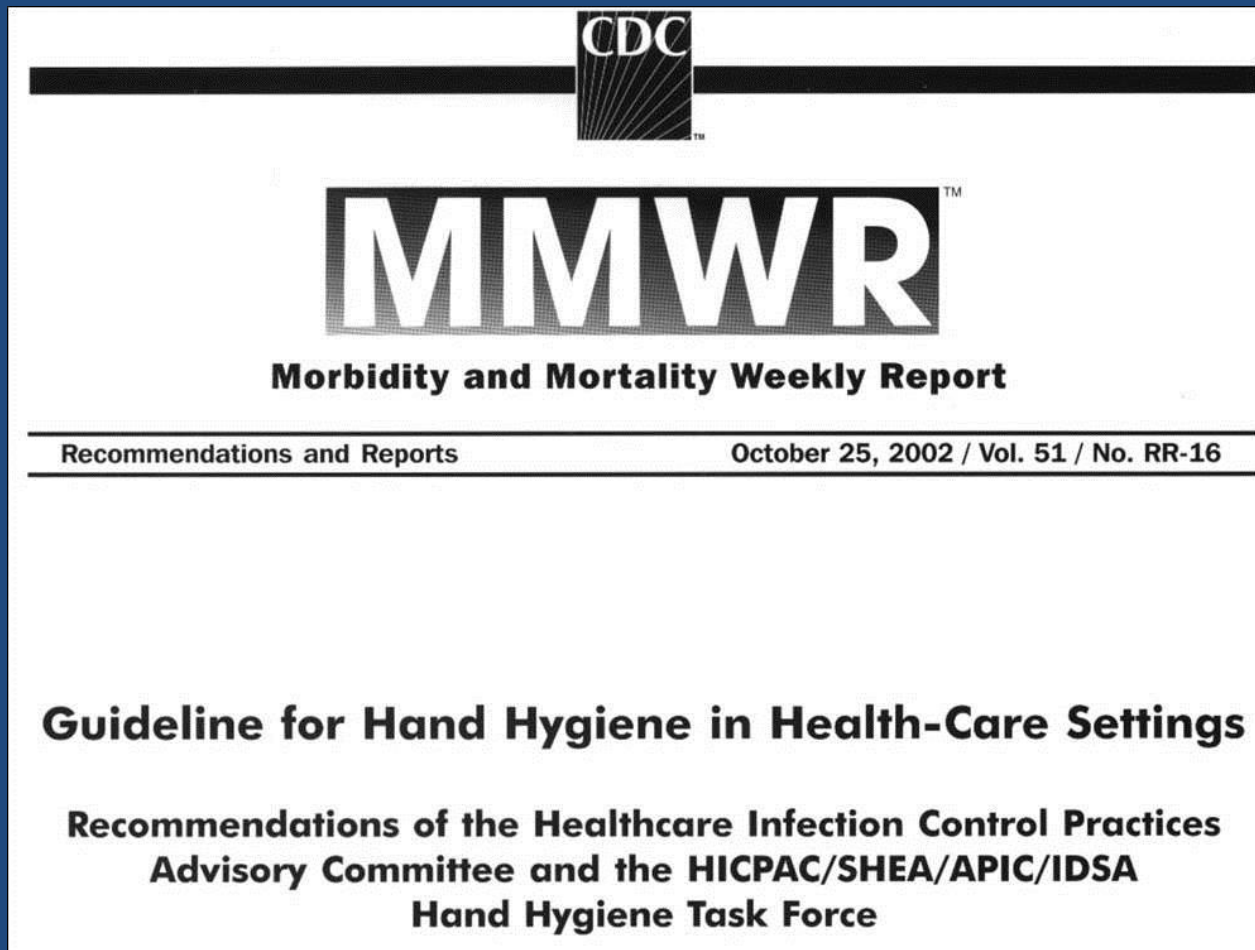
- Oral-fecal acquisition
- Diarrhea usually starting while on antibiotics
- Age and proton-pump inhibitors risk factors
- Environmental cleaning limits transmission
- Recurrence or relapse after therapy 10-25% of patients
- Post-infectious irritable bowel syndrome 10%



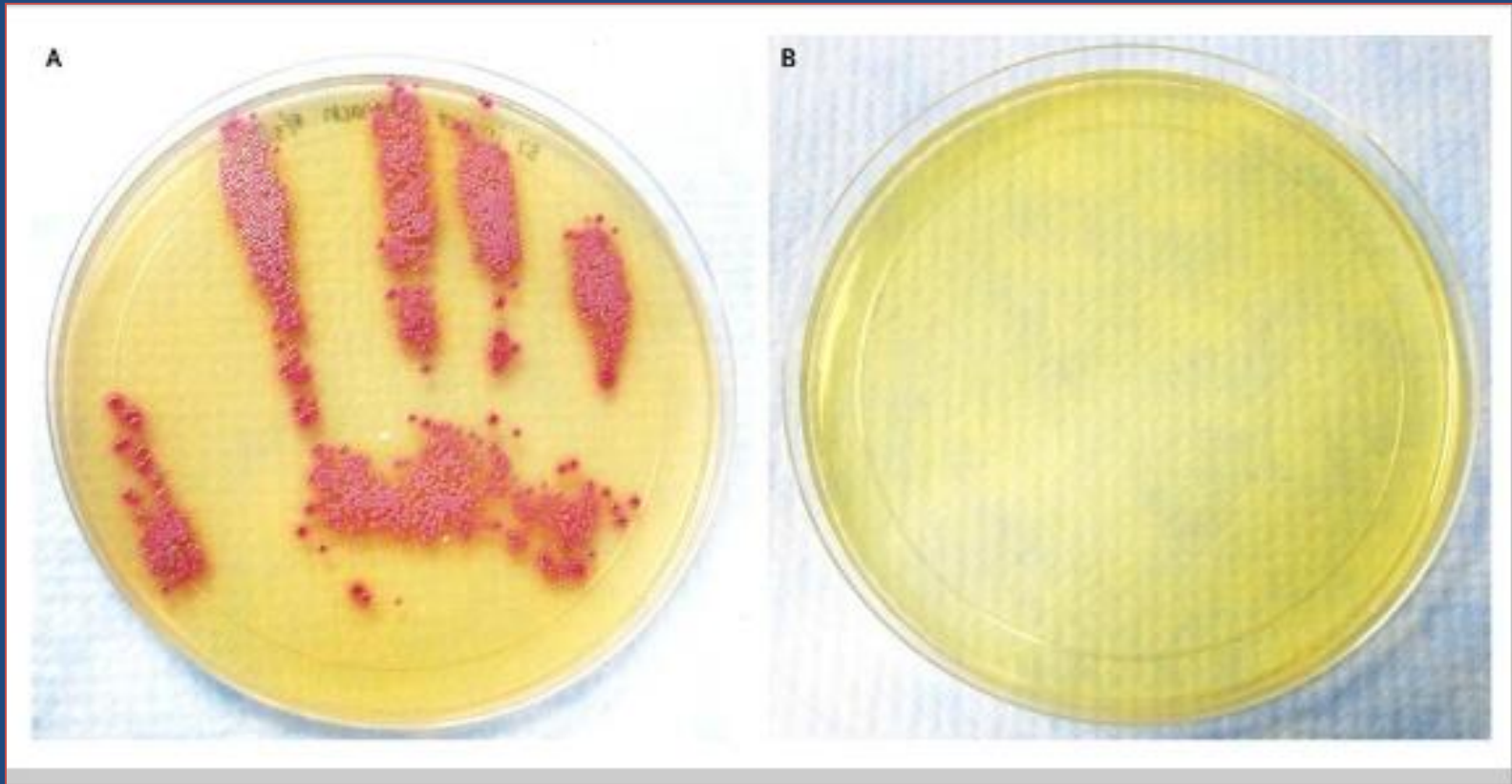
Interventions to prevent MDROs

- Hand hygiene (alcohol vs. soap)
- Active surveillance (MRSA)
- Chlorhexidine bathing
- Antimicrobial stewardship

The most essential intervention



Alcohol is good for you —



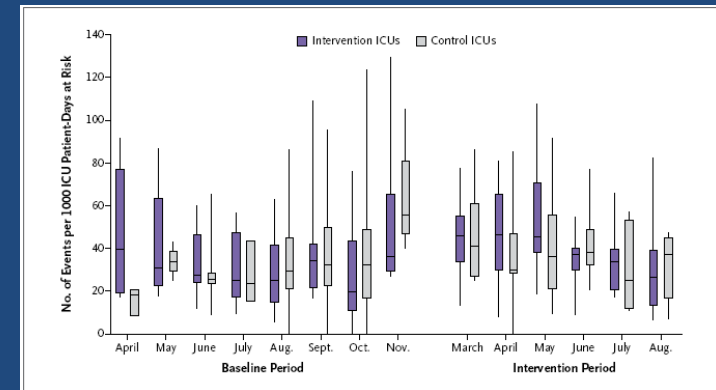
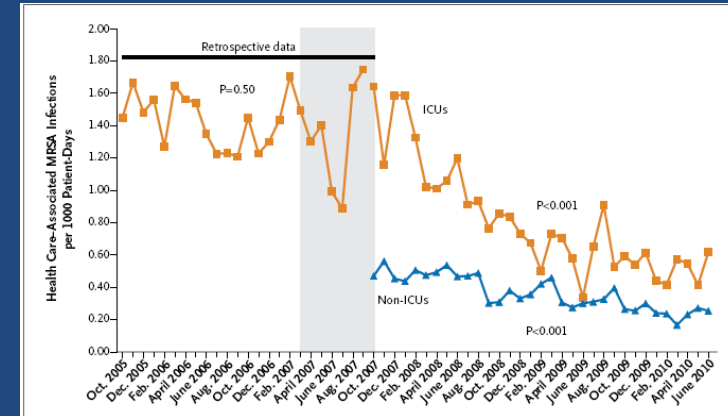
After patient contact and
before using alcohol gel

After alcohol gel

Clean your hands!

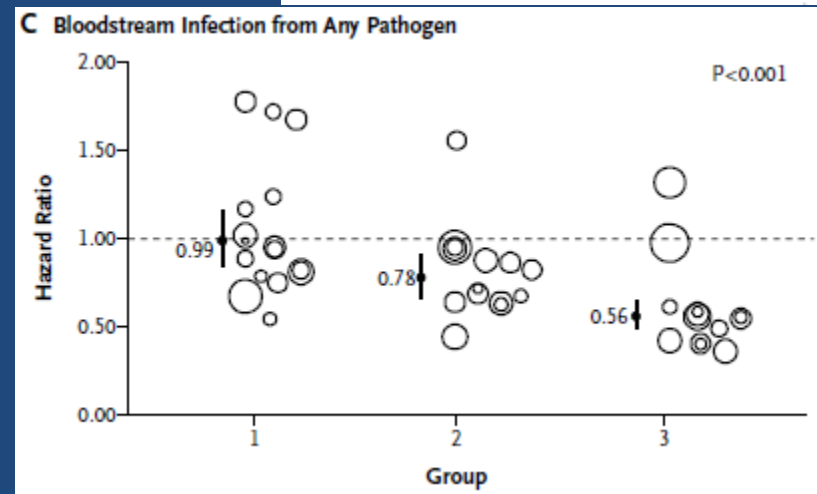
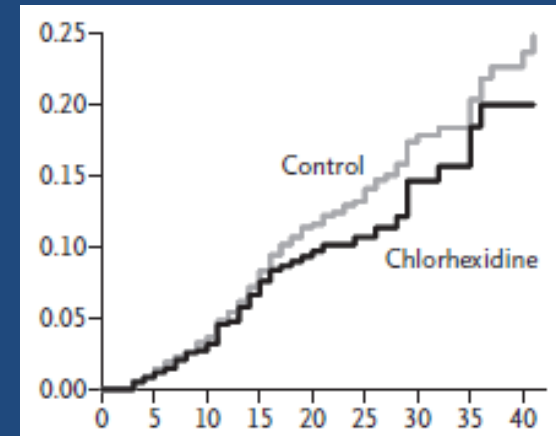
Active Surveillance Culturing

- Swabbing all patients on entry
- MRSA—nose
- VRE (or CRE)—GI tract
- Isolate + patients
- Unclear if it works, mandated in many locations



Chlorhexidine Gluconate (CHG) Bathing

- Once a day bathing with 2% CHG
- +/- mupirocin in nose
- All patients
- Reduce bacteremia
- Probably decrease
 - MRSA/VRE



Antimicrobial stewardship

- 50% of hospital antimicrobial use unnecessary
- Antimicrobial stewardship programs can decrease unnecessary use
- Probably decrease *C. difficile* and adverse drug events
- Possibly decrease resistance



QUESTION 6

Routine ICU environmental cleaning with a detergent- disinfectant (a phenolic or quaternary ammonium product) is least likely to interrupt ICU transmission of:

1. *Acinetobacter*
2. *Clostridium difficile*
3. Methicillin-resistant staphylococci
4. Vancomycin-resistant enterococci

Environmental cleaning

- The environment appears to be important for transmission of MDROs
- Hospital environments are not generally cleaned well
- Cleaning can be improved with monitoring
- Both terminal cleaning and daily cleaning are important
- Cleaning decreases *C. difficile*, VRE and likely other organisms
- Bleach for *C. difficile*
- New technology for touchless cleaning is expensive and relatively unproven

CDC Environmental Checklist for Monitoring Terminal Cleaning¹

Date:			
Unit:			
Room Number:			
Initials of ES staff (optional): ²			

Evaluate the following priority sites for each patient room:

High-touch Room Surfaces ³	Cleaned	Not Cleaned	Not Present in Room
Bed rails / controls			
Tray table			
IV pole (grab area)			
Call box / button			
Telephone			
Bedside table handle			
Chair			
Room sink			
Room light switch			
Room inner door knob			
Bathroom inner door knob / plate			
Bathroom light switch			
Bathroom handrails by toilet			
Bathroom sink			
Toilet seat			
Toilet flush handle			
Toilet bedpan cleaner			

Evaluate the following additional sites if these equipment are present in the room:

High-touch Room Surfaces ³	Cleaned	Not Cleaned	Not Present in Room
IV pump control			
Multi-module monitor controls			
Multi-module monitor touch screen			
Multi-module monitor cables			
Ventilator control panel			

Mark the monitoring method used:

☐ Direct observation ☐ Fluorescent gel ☐ Agar slide cultures
☐ Swab cultures ☐ ATP system

¹Selection of detergents and disinfectants should be according to institutional policies and procedures
²Hospitals may choose to include identifiers of individual environmental services staff for feedback purposes.
³Sites most frequently contaminated and touched by patients and/or healthcare workers

National Center for Emerging and Zoonotic Infectious Diseases
 Division of Healthcare Quality Promotion




Multidrug-resistant Organisms

		Intervention					
	Frequency	Hand Hygiene	Gown and Glove	CHG bathing	Env. Cleaning	AM Stewardship	ASC
MRSA	↓	Yes	Yes	Yes	Prob	?	Prob
VRE	↓	Yes	Yes	Yes	Yes	?	?
CRE/ CRAB	↑	Yes	Yes	Prob	?	?	?
C. difficile	↑	SOAP & WATER	Yes	?	Yes	?	?

CHG=chlorhexidine

AM = antimicrobial

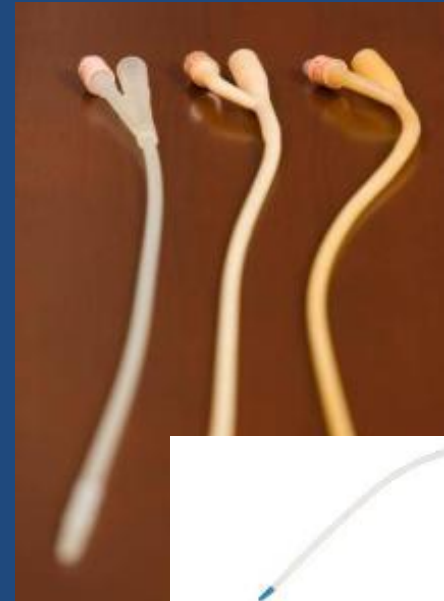
ASC = active surveillance culturing

CRE=carbapenem-R Enterobacteriaceae

CRAB=carbapenem-R Acinetobacter

Invasive devices

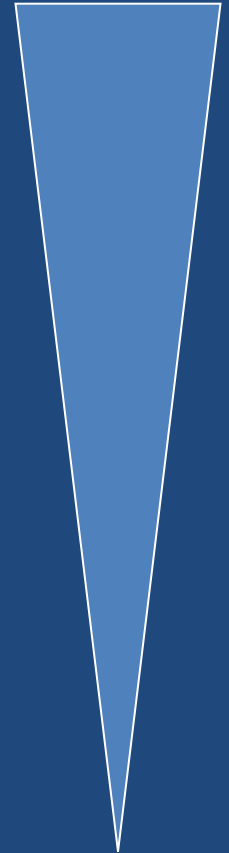
- Central venous catheters
- Endotracheal intubation
- Urinary catheters



How to prevent device infections

- Do not use device
- Remove device as soon as possible
- Insert device in proper fashion
- Perform routine care of device
- Use antibiotic/antiseptic compounds on devices
(biopatch/antibiotic impregnated materials)

Most Important



Least Important

How to prevent device infections:

Removal of devices

Ways this can be improved are:

- Daily nursing checklist reminders
- Electronic Reminders
- Public reporting—Surgical Care Improvement Project (SCIP) (Urinary catheter must have an indication if left in > 48 hours after surgery. Public reporting of rates)

QUESTION 7

Which of the following measures is least likely to reduce a patient's risk of ventilator-associated pneumonia?

1. Oral decontamination with chlorhexidine
2. Use of sub-glottic suctioning
3. Spontaneous breathing trials
4. Elevation of the head of the bed to 45°
5. Change of ventilator circuit tubing q 3 days

Preventing Ventilator-Associated Pneumonia and Other Complications

General:

- Hand hygiene for HCWs
- Aseptic care of equipment
- Daily “Sedation Vacation” and readiness to extubate

Prevent Aspiration:

- Elevation of head of bed to 30-45 degrees
- Closed suctioning? Sub-glottic suctioning — better evidence

Reduce colonization of aerodigestive tract:

- Oral decontamination (chlorhexidine)
- Avoid Peptic ulcer disease prophylaxis
- Frequency of tubing change not an issue

- Deep vein thrombosis prophylaxis (unless contraindicated)

CDC/HICPAC & Institute for Healthcare Improvement (IHI) 2005; SHEA/IDSA 2008.

The VAP Prevention Paradox

	VAP Rates	Vent LOS	ICU LOS	Hospital LOS	Death
Head-of-bed elevation					
Regular oral care with chlorhexidine					
Continuous aspiration of subglottic secretions					
Silver-coated endotracheal tubes					

QUESTION 8

- A 57 y.o. man on day 6 of ventilator/MICU stay develops 104°F fever, new pulmonary infiltrates, and new leukocytosis.

Which of the following antimicrobial regimens is most appropriate?

1. Ceftriaxone
2. Ceftriaxone & azithromycin
3. Imipenem & vancomycin
4. Imipenem & daptomycin
5. Moxifloxacin

Risk Factors for MDR VAP

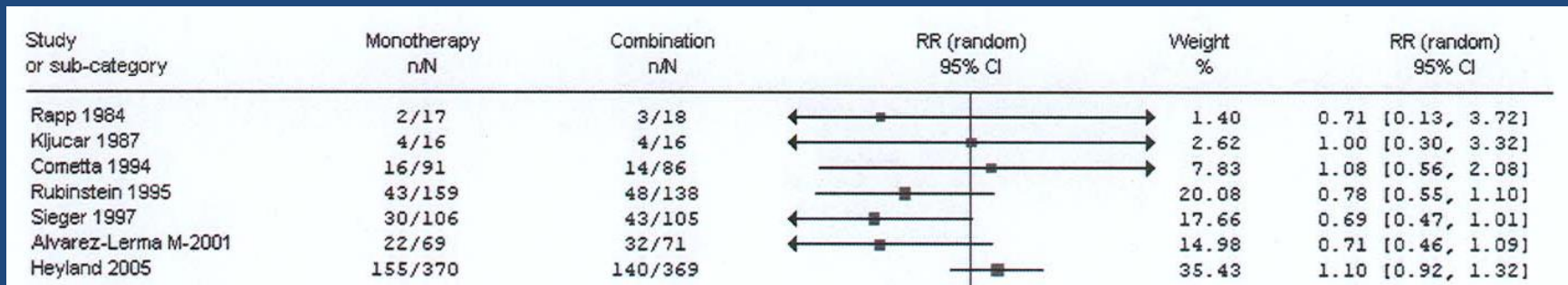
- Prior Antimicrobial therapy
- ≥ 5 days in hospital
- High frequency of antibiotic resistance
- Immunosuppressive disease and/or therapy

Antibiotics for VAP with possible MDRO

	Major organism	Antibiotics
Gram positive	MRSA	Vancomycin or Linezolid NOT Daptomycin
Gram negative	Pseudomonas	Cefepime
	Partially resistant Enterobacteriaceae (ESBL)	Pipracillin/tazobactam Imipenem +/- Fluoroquinolone aminoglycoside
	Acinetobacter	
	Legionella	Azithromycin or fluoroquinolone
	MDR/XDR gram negative suspected (CRE)	colistin

Does Use of Combination Therapy (e.g., Double-coverage) Improve VAP Outcomes?

Treatment Failure in Pooled Trials Comparing Monotherapy with Combination Therapy



Combination therapy increases chances of covering MDRO, no Synergy benefit

There was no evidence that combination therapy results in lower rates of treatment failure but rather a statistically non-significant trend to higher rates of treatment failure when combination therapy is used.
RR, relative risk; *CI*, confidence interval.

How Long to Treat VAP?

Comparison of 8 vs 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults A Randomized Trial

Jean Chastre, MD

Context The optimal duration of antimicrobial treatment for ventilator-associated pneumonia (VAP) is unknown. Shortening the length of treatment may help to con-

Treat 1 week unless *Pseudomonas* or MRSA

Dominique Perrin, MD

Fabienne Fieux, MD

Sylvie Aubas, MD

for the PneumA Trial Group

HOSPITALS AND PARTICULARLY intensive care units (ICUs) are faced with the emergence and rapid dissemination of multiresistant bacteria.¹⁻⁴ In some cases, the choice of potential therapies is limited or even nonexistent.⁵⁻⁸ The response to this challenge lies in a policy of prevention and better utilization of antimicrobial therapy, notably shortening the duration and decreasing the number of antibiotics given to ICU patients to contain the emergence and dissemination of such pathogens.^{3,9-12} Because of its frequency and severity,^{13,14} nosoco-

Main Outcome Measures Primary outcome measures—death from any cause, microbiologically documented pulmonary infection recurrence, and antibiotic-free days—were assessed 28 days after VAP onset and analyzed on an intent-to-treat basis.

Results Compared with patients treated for 15 days, those treated for 8 days had neither excess mortality (18.8% vs 17.2%; difference, 1.6%; 90% confidence interval [CI], -3.7% to 6.9%) nor more recurrent infections (28.9% vs 26.0%; difference, 2.9%; 90% CI, -3.2% to 9.1%), but they had more mean (SD) antibiotic-free days (13.1 [7.4] vs 8.7 [5.2] days, $P<.001$). The number of mechanical ventilation-free days, the number of organ failure-free days, the length of ICU stay, and mortality rates on day 60 for the 2 groups did not differ. Although patients with VAP caused by nonfermenting gram-negative bacilli, including *Pseudomonas aeruginosa*, did not have more unfavorable outcomes when antimicrobial therapy lasted only 8 days, they did have a higher pulmonary infection-recurrence rate compared with those receiving 15 days of treatment (40.6% vs 25.4%; difference, 15.2%, 90% CI, 3.9%-26.6%). Among patients who developed recurrent infections, multiresistant pathogens emerged less frequently in those who had received 8 days of antibiotics (42.1% vs 62.0% of pulmonary recurrences, $P=.04$).

Conclusions Among patients who had received appropriate initial empirical therapy, with the possible exception of those developing nonfermenting gram-negative bacillus infections, comparable clinical effectiveness against VAP was obtained with the 8- and 15-day treatment regimens. The 8-day group had less antibiotic use.

JAMA. 2003;290:2588-2598

www.jama.com

Complications of Mechanical Ventilation — The CDC's New Surveillance Paradigm

Michael Klompas, M.D., M.P.H.

The CDC's New Surveillance Paradigm for Ventilator-Associated Events.

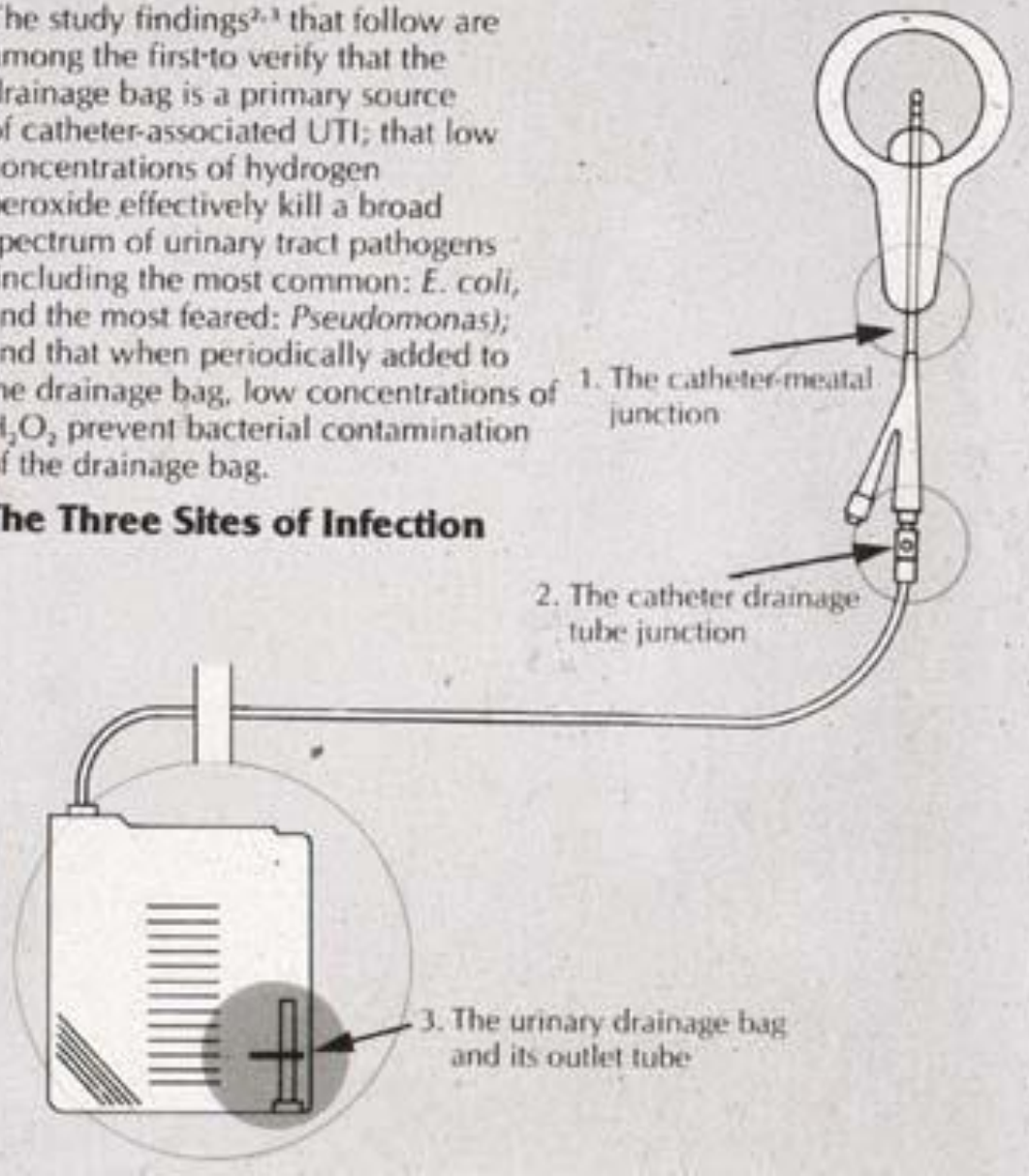
Concept	Name	Definition
New respiratory deterioration	Ventilator-associated condition (VAC)	≥2 Calendar days of stable or decreasing daily minimum positive end-expiratory pressure or daily minimum fraction of inspired oxygen, followed by a rise in daily minimum positive end-expiratory pressure of ≥3 cm of water or a rise in the daily minimum percentage of inspired oxygen by >20 points

New definition to replace VAP that is more objective, shouldn't be on the boards

New respiratory deterioration with probable evidence of pulmonary infection	Probable pneumonia	days before or after onset of a VAC, excluding the first 2 days of mechanical ventilation IVAC plus Gram's staining of endotracheal aspirate or bronchoalveolar lavage showing ≥25 neutrophils and ≤10 epithelial cells per low-power field, plus endotracheal aspirate with ≥10 ⁵ colony-forming units per milliliter or bronchoalveolar-lavage culture with ≥10 ⁴ colony-forming units per milliliter, or endotracheal-aspirate or bronchoalveolar-lavage semiquantitative equivalent, within 2 calendar days before or after onset of a VAC, excluding the first 2 days of mechanical ventilation
---	--------------------	---

The study findings^{2,3} that follow are among the first to verify that the drainage bag is a primary source of catheter-associated UTI; that low concentrations of hydrogen peroxide effectively kill a broad spectrum of urinary tract pathogens (including the most common: *E. coli*, and the most feared: *Pseudomonas*); and that when periodically added to the drainage bag, low concentrations of H_2O_2 prevent bacterial contamination of the drainage bag.

The Three Sites of Infection



- Avoid use of catheters
- Don't open or irrigate system
- Aseptic drainage of bag
- Bag below bladder

CAUTI

- Patients with indwelling catheters will often have significant bacteriuria & pyuria without UTI
- Symptoms are key to diagnosing UTI
- Only treat asymptomatic bacteriuria in pregnant women and men undergoing TURP

Preventing Device and Procedure Infections: Essentials

- HAND HYGIENE — Alcohol is good for you
- CLABSI — CHG prep & barrier precautions; CHG cleansing; CVC removal
- VAP — Oral CHG & sedation vacations (tube removal); positioning 45°
- UTI — Closed system & catheter removal
- Silver-coatings? — Unclear benefit

INFECTION CONTROL POTPOURRI

P1: Pertussis/Influenza

A 22 y.o. presents to the ED with 6 days of severe cough, coryza and lethargy. He is admitted to the hospital for further work-up and is diagnosed with pertussis.

What type of isolation does this patient require?

- 1) Contact precautions
- 2) Droplet precautions
- 3) Airborne precautions
- 4) Droplet and contact precautions

Pertussis/Influenza Answer

DROPLET PRECAUTIONS

To prevent the spread of infection,
anyone* entering this room **MUST** wear



Surgical Mask

N-95 Respirators **SHOULD NOT**
be used for personal protection
with patients in droplet precautions.

Droplet precautions
(i.e. wear surgical mask)

P2: Bronchoscopy

A pulmonary fellow is performing a bronchoscopy on a patient with influenza. What type of personal protective equipment should she be wearing?

1. Contact
2. Droplet
3. Airborne
4. Gown and glove + N95 + eye protection

Answer

- Gloves, gown, and eye protection (as part of standard precautions)
- +
- Respiratory protection equivalent to a fitted N95 respirator or equivalent during aerosol-generating procedures



P3: Contact Precautions

In which situation can Contact Precautions be removed?

-
- 1) MRSA +, negative culture on antibiotics
 - 2) *C. difficile*, diarrhea resolved
 - 3) MRSA +, negative surveillance cultures
 - 4) CRE+, negative culture during hospitalization

Answer: contact precautions can be removed when-

- **MRSA:** 3 negative cultures weekly off antibiotics
- ***C. difficile*:** diarrhea resolved
- **CRE/VRE:** guidelines unclear, but likely prolonged carriage

Duration of Colonization

- **MDR-GN**
 - Often colonized with multiple species
 - Persistence > 1 year
- Clearance Rare (GI organisms)
- **VRE**
 - Few long term studies
 - Persistence > one year
 - Antibiotics cause re-emergence

P4: Meningococcus Question

What kind of isolation does one use for *N. meningitidis*?

- 1) Contact
- 2) Droplet
- 3) Airborne
- 4) Special isolation

Meningococcus Answer

- Droplet Precautions:

- *rationale*

- infectious particles are relatively large and fall out of the air within 3 feet of the patient

- *consist of*

- wearing **surgical masks** within 3 feet of patient
 - private room or cohorted

P5: Meningococcus Question

What is required to remove isolation for *N. meningitidis*?

- 1) Resolution of fever
- 2) Discharge from the hospital
- 3) At least 1 day of therapy
- 4) End of symptoms

Meningococcus Answer

3) 24 hrs of antibiotic therapy required to remove Droplet Precautions

P6: Meningococcus Question

Over the weekend, an internist calls for advice. An outpatient with pharyngitis had a throat culture that is now growing *N. meningitidis*.

What should she do?

- 1) Nothing
- 2) Treat with penicillin
- 3) Contact dept. of health for possible outbreak
- 4) Admit for treatment with ceftriaxone

Meningococcus Answer

1) Nothing

Pharyngeal carriage is common

- 5-10% of population in non-epidemic, crowded settings
- Person-to-person transmission occurs via large respiratory droplets
- Do not culture unless disease is suspected

P7: Prophylactic antibiotics

You are called and asked what prophylaxis should a woman who lives with a patient with meningococcal meningitis receive?
(She is 24 weeks pregnant)

- 1) Ceftriaxone
- 2) Rifampin
- 3) Ciprofloxacin
- 4) Piperacillin/tazobactam

Meningococcus Answer

1) Ceftriaxone

Prophylactic antibiotics

- Ciprofloxacin
 - 500 mg po x 1 dose (adults)
- Rifampin
 - 600 mg po Q12 hours x 4 doses (adults)
 - 10 mg/kg po Q12 hours x 4 doses (children)
- Ceftriaxone—safest drug in Pregnancy
 - 250 mg im x 1 dose (adults)
 - 125 mg im x 1 dose (children)

RARE *N. meningitidis* resistance to ciprofloxacin—
Minnesota/Wisconsin/California

TB

P8: TB Discontinue Precautions

A 70 year-old Indian man presented with night sweats, cough and a right upper lobe pulmonary lesion. He is placed in Airborne Precautions for suspected pulmonary TB.

What is required before precautions be discontinued?

- 1) Negative AFB sputum smear
- 2) 3 consecutive negative AFB sputum smears
- 3) Nothing, isolation not required
- 4) Until cough resolved

TB Discontinue Precautions

- Airborne Precautions can be discontinued when TB is no longer considered likely AND (at least 1 of the following):
- An alternate diagnosis is found
 - OR
- There are 3 consecutive direct smears obtained at 8 to 24 hour intervals are negative for AFB

P9: TB Exposure

A 28 year-old pulmonary fellow performed a bronchoscopy on a patient later found to have pulmonary TB infection; at the time of care TB status was unknown and PPE was not worn.

What should he do?

- 1) Stop work
- 2) Begin one drug anti-TB medication
- 3) Undergo PPD/Quantiferon testing
- 4) Begin four drug anti-TB medications

TB Exposure

The fellow should:

- a) Receive a baseline TB screening test (TST) and if negative the test should be repeated in 8-12 weeks.
- b) Assuming the baseline screen is negative, the fellow is not considered infectious and can continue working.

P10: TB Conversion

10 weeks after the exposure, the above pulmonary fellow returns for a follow-up TB screening test. An 11 mm induration is noted 48 hours after PPD placement (there was no induration at baseline).

How should the fellow be managed?

- 1) Should stop working
- 2) Start 4 drug anti-TB regimen
- 3) Perform sputum smears
- 4) Be assessed clinically

TB Conversion

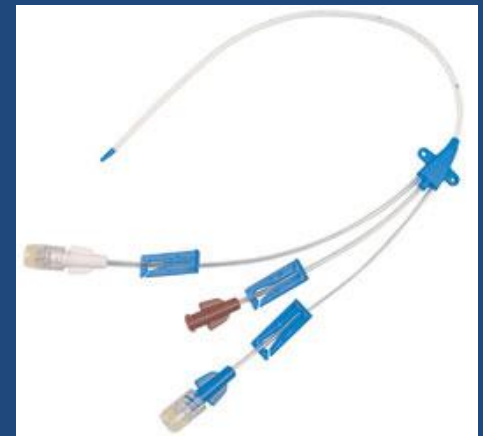
- This is considered a positive TST due to recent infection. Persons with recent TST conversions are at increased risk for developing active MTB infection.
- He should be evaluated clinically to rule out active TB and treatment for latent TB infection should be considered.
- Work restrictions are not necessary as long as fellow remains asymptomatic.

Line Sepsis: Prevention & Management

Daniel J. Morgan MD, MS
University of Maryland School of Medicine
VA Maryland Healthcare System
August 10, 2013

Central line-associated blood stream infection (CLABSI)

- Infection of a central venous catheter
- High mortality and morbidity
- Longer length of stay in hospital with higher hospital costs
- Best evidence for preventability among HAIs



QUESTION 1

A 49 year old man has acute myocardial infarction and has a CVC placed to deliver medications. On hospital day 4 he has a fever to 101oF with bacteremia. What is the most likely organism?

- 1) *E. coli*
- 2) Coagulase-negative *Staphylococcus*
- 3) *Candida* species
- 4) Vancomycin-resistant *Enterococcus*
- 5) *Staphylococcus lugdenensis*

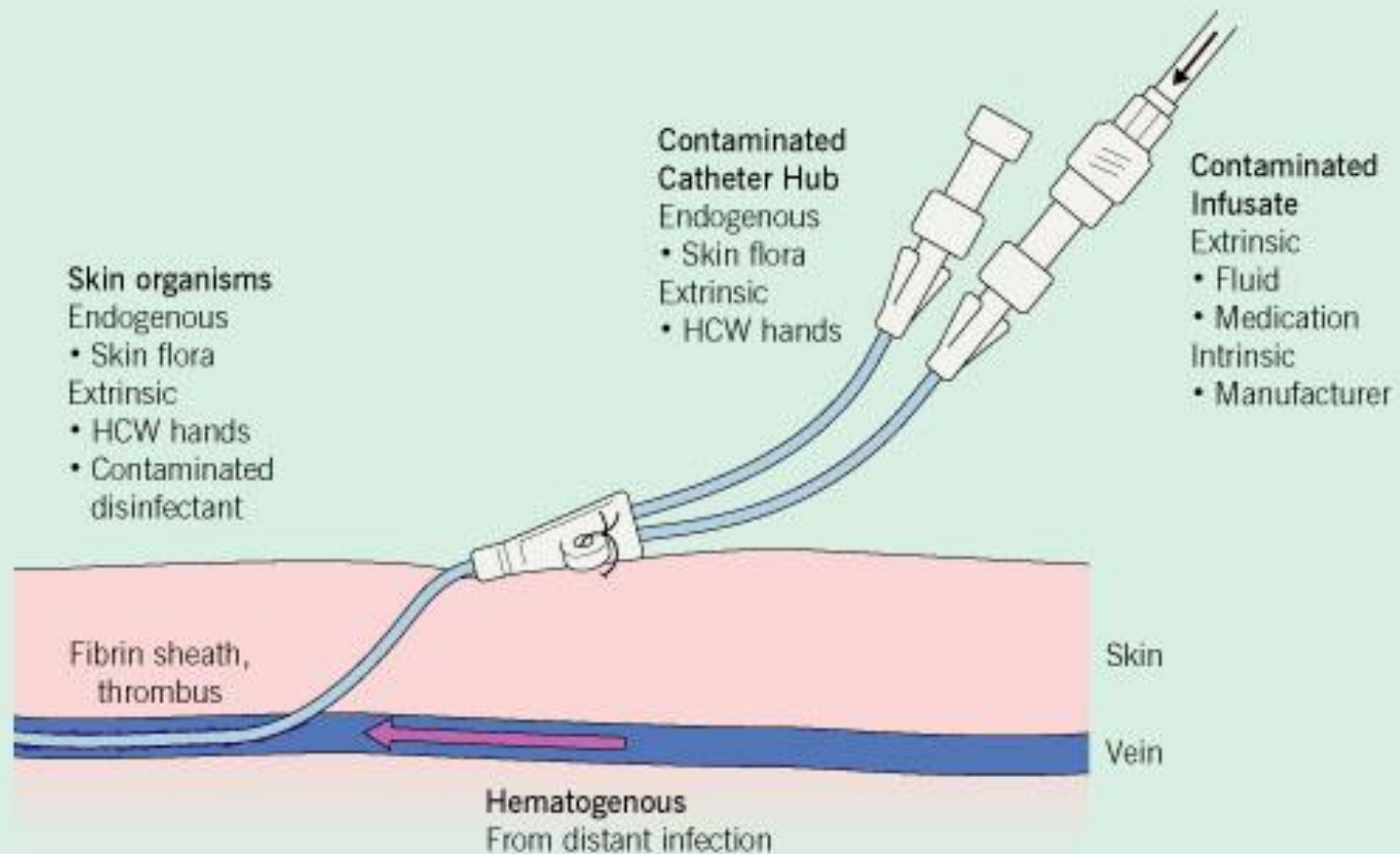
Organisms causing CLABSI

- Coagulase-negative Staphylococcus most common

But true infections probably mostly:

- *Staphylococcus aureus*
- *Candida* species
- Gram-negative bacteria (*E. coli*, *Klebsiella*, *Acinetobacter*)

POTENTIAL SOURCES OF INFECTION OF A PERCUTANEOUS INTRAVASCULAR DEVICE (IVD)



Potential sources of infection of a percutaneous intravascular device (IVD). These include contiguous skin flora, contamination of the catheter hub and lumen, contamination of infusate and hematogenous colonization of the IVD from distant, unrelated sites of infection. HCW, health care worker. Adapted from Crnich and Maki, *Clin Infect Dis* 2002; 34:1232-4.

Vascular Catheter Infection Source — Pathogenesis Mnemonic

Short-term vascular catheters — Skin

Long-term vascular catheters — Lumen

How to prevent CLABSI: Insertion

- Don't use central venous catheter and remove as soon as possible
- If using a catheter, perform sterile insertion – **Checklist!**
 - Hand hygiene
 - Clean site with chlorhexidine
 - Use full drape—covers patient's body
 - Wear surgical gown and surgical mask
 - Avoid femoral insertion site (SC>IJ)
- Line carts or line trays



How to prevent CLABSI:

Maintenance care

- Ask:
 - Is the line still necessary?
 - Does the dressing need to be changed?
 - Does tubing and connector need to be changed?
- Scrub the hub with alcohol for 15 seconds before using



How to prevent device infections: Antibiotic/antiseptic compounds

- Chlorhexidine disk at line exit site (Biopatch)
- Antibiotic impregnated catheters (minocycline-rifampin etc.)



Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011

Naomi P. O'Grady, M.D.¹, Mary Alexander, R.N.², Lillian A. Burns, M.T., M.P.H., C.I.C.³, E. Patchen Dellinger, M.D.⁴, Jeffery Garland, M.D., S.M.⁵, Stephen O. Heard, M.D.⁶, Pamela A. Lipsett, M.D.⁷, Henry Masur, M.D.¹, Leonard A. Mermel, D.O., Sc.M.⁸, Michele L. Pearson, M.D.⁹, Issam I. Raad, M.D.¹⁰, Adrienne Randolph, M.D., M.Sc.¹¹, Mark E. Rupp, M.D.¹², Sanjay Saint, M.D., M.P.H.¹³ and the Healthcare Infection Control Practices Advisory Committee (HICPAC)¹⁴.

O'Grady et al, *Clin Infect Dis* 2011; 52(9):e162–93.

<http://cid.oxfordjournals.org/content/early/2011/04/01/cid.cir257.full.pdf+html>

<http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf>

QUESTION 2

You are designing a CLABSI prevention program for your ICU. Which of the following is most important to include?

-
1. Screening for VRE
 2. Iodoophore for site preparation
 3. Full sterile drape during insertion
 4. Separate policies for placement of femoral vs. subclavian/internal jugular lines
 5. Placing central lines in the operating room

and causes of CLABSI 2001-2009

- ICU patients nationwide
- 43,000 CLABSIs to 18,000
- 58% reduction
- Reductions in *S. aureus* more marked than GNR, *Candida* and *Enterococcus*

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Leonard A. Mermel,¹ Michael Allon,² Emilio Bouza,³ Donald E. Craven,³ Patricia Flynn,⁴ Naomi P. O'Grady,⁵ Issam I. Raad,⁶ Bart J. A. Rijnders,¹⁰ Robert J. Sherertz,⁷ and David K. Warren⁸

¹Division of Infectious Diseases, Warren Alpert Medical School of Brown University, Providence, Rhode Island; ²University of Alabama-Birmingham Hospital, Birmingham, Alabama; ³Tufts University School of Medicine, Lahey Clinic Medical Center, Burlington, Massachusetts; ⁴St. Jude Children's Research Hospital, Children's Infection Defense Center, Memphis, Tennessee; ⁵National Institutes of Health, Critical Care Medicine Department, Bethesda, Maryland; ⁶Section of Infectious Diseases, University of Texas-Cancer Center, Houston; ⁷Section of Infectious Diseases, Wake Forest University School of Medicine, Winston-Salem, North Carolina; ⁸Division of Infectious Diseases, Washington University School of Medicine, St. Louis, Missouri; ⁹Servicio de Microbiología Clínica y E. Infecciosas Hospital General "Gregorio Marañón," Madrid, Spain; and ¹⁰Internal Medicine and Infectious Diseases, Erasmus University Medical Center, Rotterdam, the Netherlands

These updated guidelines replace the previous management guidelines published in 2001. The guidelines are intended for use by health care providers who care for patients who either have these infections or may be at risk for them.

EXECUTIVE SUMMARY

Diagnosis: Intravenous Catheter Cultures

General

1. Catheter cultures should be performed when a catheter is removed for suspected catheter-related bloodstream infection (CRBSI); catheter cultures should not be obtained routinely (A-II).
2. Qualitative broth culture of catheter tips is not recommended (A-II).
3. For central venous catheters (CVCs), the catheter

tip should be cultured, rather than the subcutaneous segment (B-III).

4. For cultures of an anti-infective catheter tip, use specific inhibitors in the culture media (A-II).

5. Growth of >15 colony-forming units (cfu) from a 5-cm segment of the catheter tip by semiquantitative (roll-plate) culture or growth of >10² cfu from a catheter by quantitative (sonication) broth culture reflects catheter colonization (A-I).

6. When catheter infection is suspected and there is a catheter exit site exudate, swab the drainage to collect specimens for culture and Gram staining (B-III).

Short-term catheters, including arterial catheters.

7. For short-term catheter tip cultures, the roll plate technique is recommended for routine clinical microbiological analysis (A-II).

8. For suspected pulmonary artery catheter infection, culture the introducer tip (A-II).

Long-term catheters

9. Semiquantitative growth of <15 cfu/plate of the same microbe from both the insertion site culture and

Received 16 March 2009; accepted 18 March 2009; electronically published 2 June 2009.

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

Reprints or correspondence: Dr. Leonard Mermel, Div. of Infectious Diseases, Rhode Island Hospital, 593 Eddy St., Providence, RI 02903 (lmermel@lifespan.org).

Clinical Infectious Diseases 2009;49:1-45

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1058-4838/2009/4901-0001\$15.00
DOI: 10.1086/599376

Mermel et al, *Clin Infect Dis* 2009; 49:1-45. http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Management%20IV%20Cath.pdf

Microbiologic Definitions of Catheter Infection

- Catheter colonization
 - >15 cfu from 5cm segment of tip (roll plate)
- Catheter infection
 - Same organism — from peripheral blood culture and catheter tip
 - Two blood cultures — catheter hub vs. peripheral — meet quantitative ($3 \times >$)
 - differential time to positivity (2 h earlier) criteria

But

- “two cultures of blood from peripheral sites should be evaluated because *it is difficult to determine* whether a positive culture of blood from a central venous catheter indicates contamination of the hub, catheter colonization or a CLABSI”
- Surveillance CDC definition:
 - Line + bacteremia + no other cause

Key Treatment Decisions

- Antimicrobials
- Duration of treatment
- Echocardiogram
- Remove catheter or device

Empiric Treatment Recommendations

- Vancomycin (daptomycin)— if MRSA “prevalent”
- Gram-negative coverage —local decision: susceptibility data & severity of illness
- Cover MDROs in neutropenic, very ill, or colonized patients

QUESTION 3

In which setting can a CVC be left in place despite CLABSI?

-
1. Infecting organism is *E. coli*
 2. Infecting organism is coagulase-negative *Staphylococcus*
 3. CVC is a PICC line
 4. CLABSI is in setting of endocarditis
 5. Erthyema present around external line site

Reasons to Remove Infected Catheters

- Always remove if you can (except CoNS)
 - Severe sepsis
 - Suppurative phlebitis
 - Endocarditis
 - BSI >72h into appropriate antimicrobial therapy
 - Pathogens — Gram-negative bacilli, *S. aureus*, *Enterococci*, fungi, mycobacteria

QUESTION 4

A 65 yo man is inpatient for pneumonia where he had a CVC placed for temporary hemodialysis. After renal function recovered he developed a fever and *S. aureus* was cultured from the blood. Which factor would indicate a need for treatment >2 weeks?

1. Catheter removed
2. Patient is being treated for lymphoma
3. Fever persists for >48 hours
4. Co-infection with coagulase-negative *Staphylococcus*
5. Patient debilitated and requires transfer to long-term care facility

Pathogen-specific Guidelines: Staphylococci

- CoNS — Uncomplicated catheter-related BSI:
 - Antibiotics 5-7 days if catheter removed;
 - 10-14 days if retained
- *S. lugdunensis* — Manage like *S. aureus*
- *S. aureus* — Generally remove catheter and treat 4-6 weeks
 - Short course (14+ days) if
 - catheter removed
 - patient non-diabetic & non-immunocompromised, no hardware
 - negative U/S & TEE
 - fever and BSI resolved within 72 hours of initiation of ABX
 - no signs/symptoms of metastatic infection
 - If positive catheter tip but negative peripheral blood cultures, 5-7 day systemic antibiotics with careful F/U

Pathogen-specific and General Guidelines

- Enterococci or gram-negative bacilli: 7-14 days*
- Candida: 14 days
 - Indications to cover Candida:
 - Sepsis & TPN
 - broad-spectrum antibiotics
 - hematologic malignancy/transplant
 - “multiple sites” colonization
 - Candida coverage:
 - Echinocandin
 - fluconazole (acceptable if no azole x3 months and *C. krusei* & *C. glabrata* “very low risk”)
 - 4-6 weeks if complicated infection

Echocardiogram Guidelines

- *S. aureus* shorter course (than 4-6 weeks):
TEE
- Other pathogens — be guided by clinical picture; persistent fever or BSI; presence of vascular foreign bodies
- TEE timing: at least 5-7 days after onset BSI
- Repeat TEE if earlier study negative but unexplained persistent fever or BSI persists >72h after catheter removal
- TTE inadequate to exclude endocarditis

QUESTION 5

You are treating a patient with a CVC in place for hemodialysis who develops *S. aureus* bacteremia (MSSA).

What is the best agent?

- 1) Vancomycin
- 2) Daptomycin
- 3) Nafcillin
- 4) Trimethoprim/sulfamethaxazole
- 5) Piperacillin/tazobactam

Treatment of MSSA

Methicillin-susceptible *S. aureus* (MSSA)

- Nafcillin/cefazolin > vancomycin

Taper to treat specific organism!

Catheter Infection Don'ts

- Don't culture catheter tips unless removed for suspected infection
- Don't under fill blood culture bottles (because positivity rates $\approx$ amount sampled)
- Don't start antibiotics without (re)culturing blood (peripheral & through catheter)
- Don't use linezolid for suspected catheter-related BSI
- Don't routinely reculture after d/c therapy (except infected dialysis catheters)

QUESTION 6

As a new attending at your new job, on rounds the resident informs you of a second patient in one week with *Enterobacter sakazakii* bacteremia.

What is the best response:

- 1) This must be a new organism, treat based on susceptibilities
- 2) Assume patients were in contact and acquired same bacteria
- 3) Be worried about a common source outbreak
- 4) Start 2% chlorhexidine body washes
- 5) Things are different in Arizona, this must be the reason for the big signing bonus

Epidemic CVC Infection

- Suspect outbreak with cluster of atypical organisms
 - Pseudomonas or Burkholderia spp
 - Enterobacter spp
- Often related to IV fluids or medication contamination
- Assess clonality of bloodstream or catheter isolates (e.g., antibiogram, typing results)
- Case-control study

Summary CLABSI

- Prevention
 - Don't use, insertion checklist, line care
- Organisms
 - CoNS > *S. aureus* > *Enterococcus*
- Treatment
 - *S. aureus*, justify 2 weeks (4-6 wks normal)
 - Target ABX to organism
 - Don't continue double coverage

Needlesticks

QUESTION 7

During insertion of a CVC in a patient with Hepatitis C and HIV, the resident you're supervising stuck you with lidocaine needle after using it on the patient.

The best management is:

- 1) nothing more than wash with soap & water
- 2) inteferon & ribavirin
- 3) Truvada (emtricitibine/tenofovir)
- 4) Truvada, Interferon & ribavirin
- 5) Advise the resident to go into ID where manual dexterity not as important

Was it an exposure to a Blood Borne Pathogen (BBP)?

- Percutaneous (e.g. needlestick)
- Mucous membrane (e.g. eyes, mouth, lips)
- Skin (non-intact or prolonged, high volume contact)
- Exposure to blood or a blood tinged body fluid or tissue
 - Most other body fluids (e.g. csf, pleural, amniotic fluids)
- Non-bloody urine, sweat or feces are not regarded as BBP exposures

The risks

<i>Source Patient with:</i>	Needlestick injuries	Mucocutaneous Exposure
Hepatitis B sAg (and HCW non-immune)	1.9- >40% (~30%)	>>0
Hepatitis C	2.7- 10% (~3%)	>0
HIV	0.2 - 0.4% (~0.3%)	>0

Considerations when using PEP for HIV



Postexposure prophylaxis (PEP)

- Hep B—if employee + titer, nothing
- Hep C—nothing, follow
- HIV—based on exposure risk
 - Low risk—Truvada (emtricitibine/tenofovir)
 - High risk—lopinavir (PI)